

May 2012

## NIEHS Spotlight



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### [Senator Reed visits SRP at Brown University](#)

U.S. Senator Jack Reed (D-R.I.), visited the Brown University Superfund Research Program April 9.



### [Veteran grantee wins Tyler Prize for Environmental Achievement](#)

Kirk Smith, Ph.D., is one of two winners of this year's coveted Tyler Prize for Environmental Achievement, the organization announced March 20 in a press release.



### [Former staff fellow to head UMES](#)

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### [ONES awardees elected to American Society for Clinical Investigation](#)

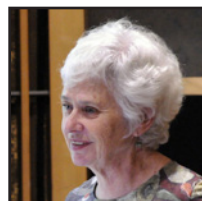
Two NIEHS-funded investigators, Brent Carter, M.D., and John Hollingsworth, M.D., received an honor that recognizes exceptional early career accomplishments.

## Science Notebook



### [Keith Yamamoto delivers 2012 Rodbell Lecture](#)

Keith Yamamoto, Ph.D., continued an annual tradition of outstanding Rodbell lectures with his seminar April 10, titled "Cell-, Gene-, and Physiology-Specific Regulation by the Glucocorticoid Receptor."



### [Spirit Lecture honors accomplished female scientist Gail Martin](#)

In recognition of Women's History Month, University of California, San Francisco professor Gail Martin, Ph.D., delivered the 2012 NIEHS Spirit Lecture April 16.



### [NIEHS scientist wins top rating at cancer conference](#)

NIEHS Staff Scientist Harriet Kinyamu, Ph.D., won a poster prize at the American Association for Cancer Research annual meeting March 31-April 4 in Chicago.



### [Science writers learn about NIEHS nano program](#)

NIEHS Health Scientist Administrator Sri Nadadur, Ph.D., delivered the American Scientist's lunchtime seminar March 27 at Sigma Xi headquarters in RTP.

## NIEHS Spotlight



### [Presidential advisor discusses Health Data Initiative](#)

U.S. Department of Health and Human Services Chief Technology Officer Todd Park gave a spirited talk April 5 at NIEHS about the Health Data Initiative.



### [WETP convenes its sixth National Trainers' Exchange](#)

Nearly 250 trainers from the NIEHS Worker Education and Training Program met March 28-29 to improve training methods for emergency response workers.



### [Team calls for creative approaches to accountability](#)

Librarian Cathy Sarli and bioinformaticist Kristi Holmes, Ph.D., urged scientists and administrators to think outside the citations analysis box to quantify research outcomes.



### [Former NTP counselor named to California EPA post](#)

Gina Solomon, M.D., will assume a top post with the California Environmental Protection Agency, according to a California Newswire press release April 11.



### [PEPH Evaluation Metrics Manual now available](#)

After more than three years of collaboration, the Partnerships for Environmental Public Health Evaluation Metrics Manual is finally available to the public free of charge.



### [Stem cell fellow moves to UNC](#)

Raluca Dumitru, M.D., Ph.D., will be director of the Human Embryonic Stem Cell Core Facility at the University of North Carolina at Chapel Hill.

## Science Notebook



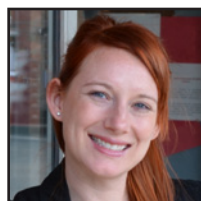
### [New studies offer insight into effects of air pollution on children](#)

Two new NIEHS-funded studies, led by researchers at Columbia University, link urban air pollution with asthma risk and behavioral problems in children.



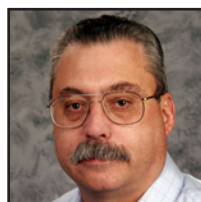
### [Temperature variability tied to shorter life expectancy](#)

NIEHS-funded researchers report that increasing variability in summer temperatures may reduce the life expectancy of elderly people with chronic medical conditions.



### [Early-life exposure to secondhand smoke affects girls more than boys](#)

The negative health effects of early-life exposure to secondhand smoke appear to impact girls more than boys—particularly those with early-life allergic sensitization.



### [Arsenic turns stem cells cancerous, spurring tumor growth](#)

NTP lead researcher Michael Waalkes, Ph.D., and his team have discovered how exposure to arsenic can turn normal stem cells into cancer stem cells.



### [Does diet alter damage from environmental exposures?](#)

What people eat may be able to determine whether or how extensively powerful chemicals, such as PCBs, damage their bodies, according to a new NIEHS-funded study.

## NIEHS Spotlight



### [Facebook and Twitter drive NIEHS social media expansion](#)

NIEHS continues to expand the reach of its environmental health message by creatively adapting it for the ever-exploding world of social media.



### [Former NIEHS fellow receives travel award](#)

Quiana Childress was selected to receive a FASEB Minority Access to Research Careers travel award to attend the Experimental Biology 2012 meeting.



### [Folt appointed interim president at Dartmouth](#) Video

Carol Folt, Ph.D., a member of the Superfund Research Program at Dartmouth College, was appointed interim president of the college April 17.



### [Trainees reach out to area students for NC DNA Day](#)

NIEHS trainees once again traded in their pipettes this April for hall passes to participate in North Carolina DNA Day.



### [Birnbaum discusses 12th ROC at congressional joint hearing](#)

NIEHS/NTP Director Linda Birnbaum, Ph.D., addressed questions regarding the NTP report April 24 during a U.S. House of Representatives joint subcommittee hearing.



### [Environmental justice advocates honored as green champions](#)

NIEHS staffers Chip Hughes, Sharon Beard, and Liam O'Fallon are being honored with the Good Neighbor Award by the U.S. Department of Health and Human Services.

## Science Notebook



### [GEMS goes transdisciplinary with spring meeting](#)

The agenda was designed to highlight emerging environmental issues — ones that are changing people's everyday lives and challenging preconceived notions.



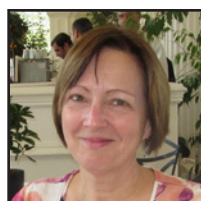
### [Harris discusses novel target to promote HIV eradication](#)

Cancer geneticist Reuben Harris, Ph.D., spoke April 16 as part of the Laboratory of Molecular Carcinogenesis Fellows Invited Guest Lecture Series.



### [BPA exposure traced to abnormal heart rhythms](#)

A new study by NIEHS grantees links the chemical bisphenol A to increased frequency of arrhythmias, or heartbeat irregularities, in animals.



### [Columbia University unveils NPL mapper](#)

NIEHS-funded researchers have developed a new online mapper capable of displaying population and environmental characteristics of areas surrounding hazardous waste sites.



### [This month in EHP](#) Audio

The lead news story in the May issue of Environmental Health Perspectives examines Shell's plans for addressing oil spills in Arctic seas.

## Inside the Institute



### [NTA meeting addresses accomplishments and concerns](#)

The NIEHS Trainees Assembly held its spring 2012 general assembly meeting April 19, highlighting its accomplishments and plans for the upcoming year.



### [Outreach staff hits the pavement during NC Science Festival](#) Video

NIEHS outreach specialists joined the tens of thousands of people who flocked to Raleigh April 20-21 for the grand opening of the new Nature Research Center.

## Extramural Research

### [Extramural papers of the month](#)

- Health implications of temperature variability
- Autism risk linked to maternal diabetes and obesity
- Potential treatment for Parkinson's disease
- Environmental estrogens and developmental reprogramming

## Intramural Research

### [Intramural papers of the month](#)

- Determining specificity for enzymes used in heparin and heparan sulfate production
- Calcium influx is a critical component of embryonic development
- Members of the Ccr4-Not complex crucial for embryonic stem cell circuitry
- Scientists link impaired lung development to Nrf2 deficiencies in neonatal mice under oxidant stress

## Calendar of Upcoming Events

- **May 3**, in Rodbell A, 10:00-11:00 a.m. — Seminar with Rich Cregari speaking on “Emerging Automotive Technology”
- **May 3-4**, in Keystone 1003AB, 9:00 a.m.-5:00 p.m. — NIEHS Centers for Neurodegeneration Science Directors’ Meeting
- **May 7**, in 101/F-193, 10:00-11:00 a.m. — Laboratory of Signal Transduction Seminar Series on “Control of Cholesterol/Lipid Homeostasis: the SREBP/miR-33 Circuit,” by Stefan Feske, M.D.
- **May 7**, in Rodbell Auditorium, 11:00 a.m.-12:00 p.m. — Laboratory of Molecular Genetics Fellows’ Invited Guest Lecture with Maureen Murphy, Ph.D., addressing “The Impact of p53 Polymorphic Variants on Cancer and Disease”
- **May 9-12 (offsite event)**, at the Raleigh (N.C.) Convention Center, 8:30 a.m.-5:00 p.m. — Society for Investigative Dermatology Annual Meeting and 75th Anniversary Celebration
- **May 9**, in Rodbell Auditorium, 10:00 a.m.-12:00 p.m. — Ethics Day with guest speakers Kevin Elliot, Ph.D., and Meave Tooher
- **May 15**, in 101/F-193, 1:00.-2:00 p.m. — Carlos de los Santos, Ph.D., speaking on “History of DNA Repair — Anecdotal Observations on the Origins of Mutation Research”
- **May 21-22**, in Rodbell Auditorium, 8:00 a.m.-5:00 p.m. — National Advisory Environmental Health Sciences Council Meeting
- **May 23**, in 101/F-193, 10:00-11:00 a.m. — Laboratory of Neurobiology Seminar Series with Ted Abel, Ph.D., topic TBA.
- **May 24**, in Rodbell C, 10:00-11:00 a.m. — Seminar on “Responding to Community Concerns on Environmental Public Health — Advancing the Scientific Research, Translation, and Policy Agenda,” by Andrea Hricko
- **May 29-30**, in Rodbell Auditorium, May 29 1:00-5:00 p.m. and May 30 9:00a.m.-12:30 p.m. — Symposium on Motif Identification and ChIP-seq Data Analysis
- View More Events: [NIEHS Public Calendar](#)

# NIEHS Spotlight

## NIEHS engages researchers and community in Boston

By Eddy Ball

With its most recent community engagement outreach initiative, NIEHS tackled the issues of asthma and air quality in communities within the city of Boston.

Led by NIEHS/NTP Director Linda Birnbaum, Ph.D., a group of NIEHS-funded researchers and Institute representatives toured Boston-area neighborhoods by trolley the afternoon of March 28. Along their route, the group saw firsthand why residents are concerned about their urban environment, along with several examples of how private-public partnerships have helped improve health and quality of life there. That evening, the group joined local government officials and public health advocates for a community forum at the Dorchester House Multi-Service Center.

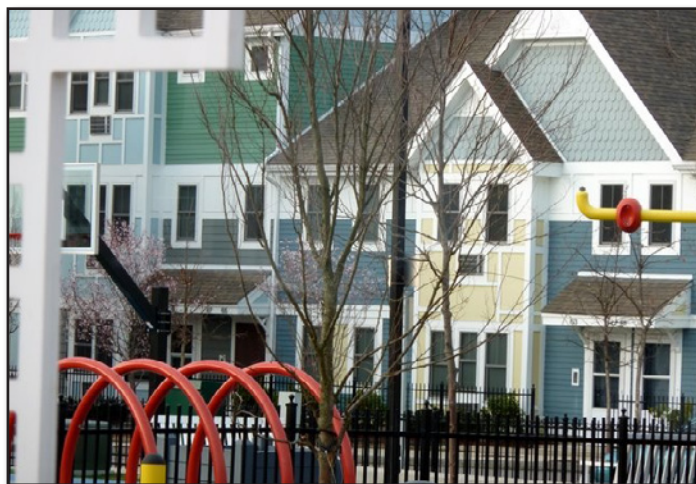
### Promoting quality of life in one of the nation's oldest cities

Accompanying the NIEHS delegation on the tour were members of NIEHS-supported Environmental Health Sciences Core Centers, who had concluded a two-day meeting in Boston. Several community members escorted the group along their route, as they visited a number of successful urban revitalization projects that have advanced environmental sustainability, fostered historical preservation, improved infrastructure, and expanded affordable housing opportunities in area communities.

The tour ranged from the renovated mixed-use historic Russia Wharf, sited near the location of the 1773 Boston Tea Party, and West Broadway, the first of Boston's Healthy Public Housing Initiatives, to intergenerational housing and community at Boston's Hope Properties, a U.S. Environmental Protection Agency remediation site that attracted \$8.5 million of additional private and public investment. One of the final locations on the tour before the group reached the Dorchester House was the Ashmont T Station,



*During their trolley tour, the group heard about the problem of pesticides in urban neighborhoods from Willie Mae Bennett-Fripp, right, Committee for Boston Public Housing executive director. "It wasn't until a bug bomb blew out the doors in public housing that the problem of chemicals became known," she said. The incident was one of several that prompted Boston to include a pesticide buyback program as a part of [integrated pest management in public housing](#). (Photo courtesy of John Schelp)*



*From the trolley, visitors could see the results of community advocacy for improvements and a smoking ban in public housing to help combat the alarming increase in asthma incidence. Advocates benefited from Harvard University environmental health surveys, lung function tests, and integrated pest management protocols in their petition to make these urban environments healthier. (Photo courtesy of John Schelp)*

a refurbished Metropolitan Boston Transit Authority intermodal station with six stories of mixed-income housing and ground floor retail space.

### **Birnbaum addresses community forum about neighborhood concerns**

In her brief introductory remarks, Birnbaum described the \$41 million NIEHS investment in health research in the state of Massachusetts, most in the greater Boston area, and the Institute's ongoing commitment to understanding and preventing the host of diseases linked to environmental contaminants. "As I see it, environmental health research is the key to preventing disease," she said, "because you can't change your genes, but you can change your environment."

After noting examples of the range of environmental influences on health, Birnbaum focused on air pollution and its role in respiratory diseases, such as asthma, cardiovascular disease, and neurodevelopment. She pointed to groundbreaking research by area scientists working at Harvard, Boston, and Tufts Universities, as well as ongoing efforts across the nation to promote environmental public health.

In closing, Birnbaum yielded the floor to community members, saying, "My team and I want to hear from you. We want to hear more about what's happening in your neighborhoods."

The NIEHS team and other members listened as residents shared their hopes and concerns about their health and the quality of life in their neighborhoods. In response to audience comments, forum panelist James Hunt, chief of Environmental and Energy Services for the city of Boston, underscored the importance of community engagement and environmental health research in becoming aware of problems and in shaping effective government interventions for public health.

"We have used this national research to change policy in the city," Hunt said. Like his colleagues, Hunt emphasized that he needs input from residents about their needs and about what government and public-private efforts can do to improve the environmental quality of area neighborhoods.



*Along the tour, visitors saw the George Robert White Environmental Conservation Center, which was built on reclaimed land in Dorchester. Programs there help neighborhood children learn about their connection to the environment. (Photo courtesy of Marilyn Hair of the University of Washington)*



*Adjacent to the center is a restored natural area in the midst of one of Boston's oldest and largest neighborhoods. (Photo courtesy of John Schelp)*



*Improvements to the built environment include a new crosswalk at Dorchester House, site of the NIEHS community forum, which makes negotiating traffic safer for pedestrians. (Photo courtesy of John Schelp)*



*Along with people from the community, the audience included directors and members of NIEHS-funded centers committed to community engagement as the foundation for environmental science research. (Photo courtesy of John Schelp)*



*Birnbaum assured the audience that NIEHS is in for the long haul. "We look forward to continuing our support for this research and working with scientists, health care providers, community members, and other partners here." (Photo courtesy of John Schelp)*



*Massachusetts Department of Public Health representative Jean Zotter, right, responded to parents' concern about their children's respiratory health. Seated beside her is public health advocate Mary White of the Boston Healthy Homes and Schools Collaborative Parents of Children with Asthma. (Photo courtesy of John Schelp)*



*Several of the panelists had no problem relating to community concerns. "I'm not an asthma expert, just a kid who grew up in Boston with asthma," remarked Boston City Councilman Felix Arroyo, left. (Photo courtesy of John Schelp)*

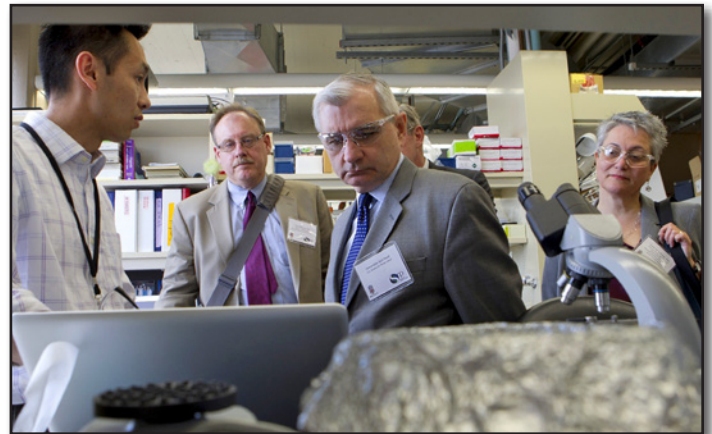


*Birnbaum, right, and other panelists spent time afterwards talking with participants in the community forum. (Photo courtesy of John Schelp)*

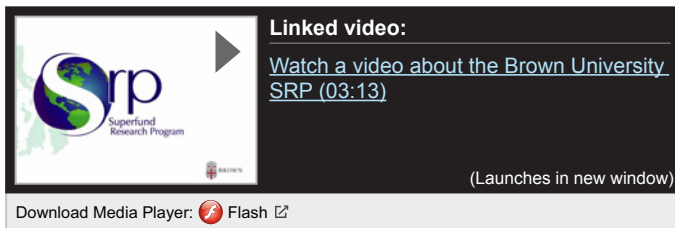
# Senator Reed visits SRP at Brown University

*By Angela Spivey*

U.S. Sen. Jack Reed, D-R.I., visited the Brown University Superfund Research Program (SRP) April 9. During a tour of the SRP facilities, Reed learned about the program's contributions to remediating contaminated sites in Rhode Island and across the country, and learned how the program is connecting with local communities and developing the next generation of environmental leaders.



*Reed, center, toured the SRP facilities at Brown. Shown above, left to right, are Edward Dere, Ph.D., a research associate in the Brown SRP, Spalding, Reed, and Collman. (Photo courtesy of Brown University)*



“Putting people to work to reduce the negative impacts of abandoned hazardous waste sites is a smart investment to protect public health, the environment, and our economy,” Reed said after the tour. “I am pleased that Brown’s federally funded Superfund Research Program is working through targeted research and community outreach, to address health concerns and design novel techniques to reduce toxic chemicals at Superfund sites in Rhode Island.”

Reed was joined by Curt Spalding, regional administrator for the U. S. Environmental Protection Agency’s New England office, and Gwen Collman, Ph.D., NIEHS Division of Extramural Research and Training director. “Senator Reed was very knowledgeable and supportive of SRP activities at Brown and of the work done by NIEHS. It was a great day,” Collman said.

The Brown University SRP works at three Superfund sites in Rhode Island. Its mission is to track the flow of hazardous gases from the contaminated sites; identify and test chemicals; clean up the contaminated sites in collaboration with community and neighborhood associations, as well as state and federal agencies; and reveal insights into how chemicals can alter human health and reproduction. In addition to working at the contaminated sites in Rhode Island, the Brown SRP connects to other Superfund sites nationwide.

“The Brown program is an outstanding one, and is a real model for integrating biomedical and nonbiomedical research, as well as translating it in a meaningful way to improve the community’s health,” said William Suk, Ph.D., director of the NIEHS Superfund Research Program. “Kim Boekelheide, [M.D., Ph.D.], and his group at Brown have kept their efforts focused on the people of Rhode Island, while at the same time their results can be applied to a variety of communities throughout the United States.”

(Angela Spivey is a contract science writer for the NIEHS Superfund Research Program.)

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# Veteran grantee wins Tyler Prize for Environmental Achievement

By Eddy Ball

NIEHS grantee Kirk Smith, Ph.D., is one of two winners of this year's coveted Tyler Prize for Environmental Achievement, the organization announced March 20 in a [press release](#).

The prize brings [Smith](#), a professor in the University of California (UC) Berkeley School of Public Health, and co-winner [John Seinfeld, Ph.D.](#), a professor of chemical engineering at the California Institute of Technology, each a \$100,000 prize and a gold medallion, which were presented at an awards ceremony April 27 in Los Angeles. On April 26, they delivered public lectures at the Davidson Conference Center at the University of Southern California, which administers the award.

In its press release, the organization explained, "Since its inception in 1973 as one of the world's first international environmental awards, the Tyler Prize has been the premier award for environmental science, environmental health, and energy, given to those who confer great benefit upon humankind through environmental restoration and achievement."

Videos of interviews with Smith and Seinfeld, as well as their lectures, are posted at <http://www.usc.edu/dept/LAS/tylerprize/video.html>.

## Indoor air pollution in the developing world

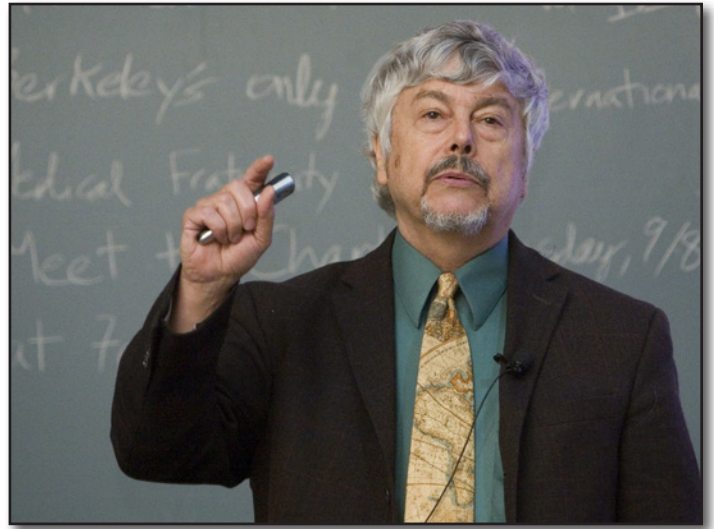
The Tyler Prize is Smith's second major award for his seminal work establishing that household air pollution in developing nations is responsible for nearly two million premature deaths per year, disproportionately among women and children. In 2009, Smith was recognized by the Heinz Foundation, which also presented him with a \$100,000 prize for his efforts to bring about a cleaner, greener, and more sustainable planet ([see story](#)).

Since the early 1980s, Smith has championed research to understand the health threat posed by particulate matter (PM) indoor air pollution, and to reduce exposures for people who heat and cook by burning biomass indoors, through development of affordable and more efficient stove technology ([see story](#) on his 2011 study in Guatemala).

Smith has received NIEHS support during his more than 30 years of research and currently holds two NIEHS grants, [Investigation of Indoor Solid Fuel and Kerosene Use as Tuberculosis Risk Factors](#) and [Estimating Dioxin Exposure from Indoor Woodsmoke and the Burning of Plastics](#).

## A premier award in the environmental health sciences

Established through an endowment by John and Alice Tyler to recognize individuals who have contributed in an outstanding manner to the scientific knowledge and public leadership to preserve and enhance the environment



*"Most people recognize that smoking is the worst thing you can do for your health," Smith was quoted as saying in the Tyler Prize press release. "The next worst thing you can do is be around smoke, and indoor fires are like being around a thousand burning cigarettes per hour. Babies may not smoke, but they are in these homes." (Photo courtesy of Kirk Smith)*

of the world, the name of the award has changed over the years, but not its purpose. Smith and Seinfeld join a list of 64 distinguished scientists and four organizations who have received the award over its nearly 40-year history.

Past winners include the following distinguished environmental scientists:

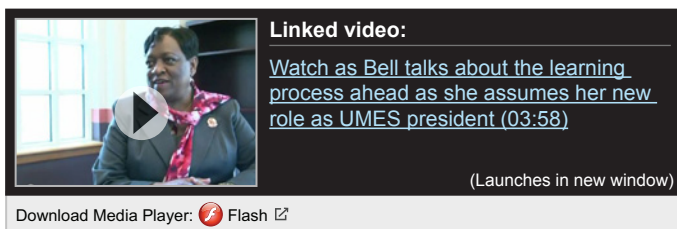
- Edward Wilson, Ph.D., recognized for his early work on the theory of island biogeography
- Jane Goodall, Ph.D., selected for her seminal studies on the behavior and ecology of chimpanzees and her impact on wildlife awareness and environmental conservation
- Jared Diamond, Ph.D., a renowned author who gave birth to the discipline of conservation biology
- Thomas Lovejoy, Ph.D., a central figure in alerting the world to the critical problem of dwindling tropical forests
- Bruce Ames, Ph.D., developer of the Ames Test for the rapid screening of environmental carcinogens

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## Former staff fellow to head UMES

*By Eddy Ball*

Biochemist Juliette Bell, Ph.D., a former NIEHS staff fellow and research biologist, will become the next president of the University of Maryland Eastern Shore (UMES) July 1, according to a [press release](#) issued in March. [Bell](#) will complete the academic year in her current position as provost and vice president for academic affairs at Central State University in Wilberforce, Ohio.



With a bachelor's degree from Talladega College and a Ph.D. from Atlanta University (now Clark Atlanta University) in chemistry, Bell became one of the first Carolina Minority Postdoctoral Scholars at the University of North Carolina at Chapel Hill in 1987, where she also received an NIH National Research Service Award. In 1990, she continued her postdoctoral studies as a staff fellow at NIEHS.

Under the guidance of NIEHS senior scientist [Thomas Kunkel, Ph.D.](#), she studied the accuracy of DNA synthesis by exonuclease-deficient *E. coli* DNA polymerase I and was one of the first to produce an exonuclease-deficient form of a eukaryotic DNA polymerase.



*Bell's commitment to service includes a position on the National Science Foundation's Biological Sciences Advisory Committee and as a consultant to the Association of American Colleges and Universities. (Photo courtesy of UMES)*

“Juliette is a dedicated and exceptional scientist,” Kunkel said of his former colleague. “But she is also a visionary who has worked hard to open doors for women and other underrepresented populations in the fields of science, technology, engineering, and mathematics. I think her new position will allow her to have an even greater impact in both pursuits.”

### **A stellar academic career**

Bell left NIEHS for a tenure track position at Fayetteville State University (FSU) in 1992, where she pursued her scientific interest with a National Science Foundation Young Investigator Award and an NIH Minority Biomedical Research Support grant. She rose quickly in the academic ranks, making full professor in 1998, as she directed first the FSU Biomedical Research Program (1993-2006) and then the Research Initiative for Scientific Enhancement (2002-2006).

In 2004, Bell began to take on more administrative duties at FSU as dean of the College of Basic and Applied Sciences, prior to assuming the roles of provost and vice chancellor for academic affairs in 2006. Following a research sabbatical in 2009, she accepted her current position at Central State University.

In recognition of her quality of teaching and leadership, Bell has received a number of awards during her career. They include being one of only four individuals in the nation to receive the Millennium Award for Excellence in Teaching from the White House Initiative on Historically Black Colleges and Universities in 2000.

She was also named a Giant in Science by the Quality Education for Minorities/Math Science Education Network and Teacher of the Year at FSU. She has earned the National Association for Equal Opportunity in Higher Education Research Excellence Award; the Minority Access, Inc., National Role Model Mentoring Award; and the prestigious University of North Carolina Board of Governors Award for Excellence in Teaching.

### **Looking forward**

“I am extremely delighted and humbled to be selected as the next president of a great institution,” Bell was quoted as saying about her appointment. “I look forward ... to continue building upon the tremendous 125-year legacy of UMES.”

One of the 13 institutions of the University System of Maryland, [UMES](#) is a land-grant university and is recognized as one of the nation’s leading historically black institutions. Located in Princess Anne, Md., the institution is well known for its distinctive array of undergraduate and graduate academic programs.

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## **ONES awardees elected to American Society for Clinical Investigation**

*By Eddy Ball*

Two NIEHS-funded investigators, Brent Carter, M.D., and John Hollingsworth, M.D., received an honor that recognizes exceptional early career accomplishments — election to the American Society for Clinical Investigation (ASCI). ASCI is a highly respected medical honor society established in 1908.

[Hollingsworth](#) and [Carter](#), who are NIEHS Outstanding New Environmental Scientist awardees, are among the group of [68 new members](#) elected to the membership in 2012. They were inducted into the society during the ASCI Dinner and New Member Induction Ceremony April 27 as part of the ASCI/American Academy of Pediatrics [joint meeting](#) in Chicago.

When he learned of the election results, Hollingsworth wrote to colleagues at NIEHS, “I think this reflects very highly on the success of the ONES program at NIEHS.”

### Early career support by NIEHS

Started in 2006, the highly competitive NIEHS ONES award is granted each year to a handful of nominees, on the basis of early-stage career promise in the field of the environmental health sciences. The award provides support for up to five years, as recipients establish their labs, research programs, and reputations, in what NIEHS hopes will be a long and productive relationship with the Institute.

Carter is an associate professor in the department of internal medicine at the University of Iowa Carver College of Medicine, with research interests in pulmonary fibrosis, asthma, and acute lung injury. Carter currently holds two NIEHS grants, [Lung Inflammation and Fibrosis After Asbestos Exposure Is Regulated by RAC1](#) and [Hydrogen Peroxide and Asbestosis](#).

Hollingsworth is an associate professor of medicine and assistant professor of immunology at Duke University Medical Center. His research program focuses on the interaction between exposure to common environmental factors and host vulnerability to complex heritable lung disease — work supported by two NIEHS grants, [Ozone Primes Pulmonary Innate Immunity](#) and [Environmental Epigenetics and Innate Immunity](#).

### ASCI – the chosen few

As the society’s website explains, “The ASCI is comprised of more than 2,800 physician-scientists from all medical specialties, elected to the society for their outstanding records of scholarly achievement in biomedical research.” The number of new members inducted each year is limited to 80 individuals under the age of 45, with only about half of the physicians nominated by members of the society being selected for membership.

ASCI publishes the *Journal of Clinical Investigation*, a peer-reviewed biomedical research journal recognized for its broad readership and impact.

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*Carter is one of seven young researchers ([see story](#)) who received ONES awards in 2007. (Photo courtesy of the University of Iowa)*

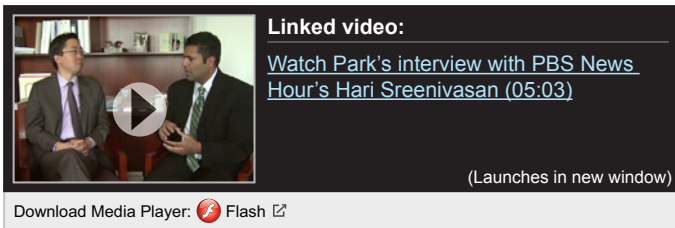


*Hollingsworth was part of a group of six scientists ([see story](#)) awarded ONES support in 2008. (Photo courtesy of Steve McCaw)*

# Presidential advisor discusses Health Data Initiative

By Ian Thomas

U.S. Department of Health and Human Services (HHS) Chief Technology Officer [Todd Park](#) gave a spirited talk to NIEHS scientists and staff about the Health Data Initiative (HDI), a monumental federal effort to make all HHS research data available to the public for electronic download. The seminar April 5 in Rodbell Auditorium outlined a wide range of programs, incentives, and competitions designed to foster healthcare innovation in both the public and private sectors. .



“By liberating all of our data for public access, we’re allowing everyone in the industry to use it as fuel for new ideas,” explained Park, who likened HDI to a similar data-sharing initiative by the [National Oceanic and Atmospheric Administration](#). “Once that happens, innovation spreads like wildfire in the form of products, services, and programs, all of which help consumers take control of their own healthcare, by putting more information at their fingertips.”

It is that sort of innovation that defines Park’s role with HHS.

“My job is to work with our smartest minds to dream up, put together, and execute, at high speed, ideas and initiatives that harness the power of data, tech, and innovation to improve the health and well-being of the American people,” said Park, who now doubles as the U.S. Chief Technology Officer and Assistant to President Obama.

## More people plus more data equals more ideas

According to Park, the major benefit of HDI is its ability to unleash massive amounts of usable health data to researchers, doctors, lawmakers, and entrepreneurs, alike, thereby allowing innovators, on all fronts, the chance to tackle problems and solutions that affect everyone.

“We have to level the playing field for everyone in healthcare to get involved,” said Park. “By creating that kind of decentralized, open data ecosystem, we will absolutely, by orders of magnitude, deliver more benefit to the public than one organization could ever produce on its own.”



*Park’s enthusiasm and humor were infectious, as he used the word awesome several times to describe the potential of integrated data for advancing a range of public and private endeavors. (Photo courtesy of Steve McCaw)*



*Park’s host was NIEHS/NTP Director Linda Birnbaum, Ph.D., who monitored the question and answer session that followed the talk. (Photo courtesy of Steve McCaw)*

## Park's Career

Prior to joining HHS in 2009, Park worked as an entrepreneur in the private sector, co-founding such companies as athenahealth, Inc., an industry leader in health information technology, and Castlight Health, a web-based health care shopping service for consumers. Park graduated magna cum laude and Phi Beta Kappa from Harvard College with a bachelor's degree in economics.

Given the amount of health data already available to users, with much more to come, NIEHS Senior Advisor [Allen Dearry, Ph.D.](#), agrees with Park's approach.

"Todd's work is extremely relevant to not only those of us at NIEHS, but everyone in the biomedical community," said Dearry. "Every day, our studies are producing more and more data and HDI gives us a framework for managing that data to its maximum potential."

### Creating a buzz

In addition to releasing all new data as open data and converting older, archived data into the same downloadable format, Park was adamant that HDI's ultimate success will likely come down to HHS' ability to publicize the data's availability once it's online.

"We have to market the bageezes out of it any way we can," Park declared, citing a number of buzz-hyping promotions, such as data paloozas and code-a-thon competitions, all of which are designed to kick-start the innovation process. "A lot of that material is already online, just waiting to be used, and yet 95 percent of the innovators in this country have no idea that it's even there."

### Expanding the issue

With the White House's recent announcement of the [Big Data Research and Development Initiative](#), a more than \$200 million effort to make government data readily accessible to the public, Park notes that the open data philosophy is by no means exclusive to healthcare.

"This same approach can, and should, be used in education, energy, and even public safety research," said Park. "Why should we limit ourselves to having only the brightest minds in government working on these problems, when we can have bright minds everywhere working on them at the same time?"

(Ian Thomas is a public affairs specialist with the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

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Several NIEHS employees, such as Chief Information Office Heather Nicholas, above, had a compelling interest in Park's talk. For Nicholas, HDI means more usable data, but also potentially a greater workload for existing resources. (Photo courtesy of Steve McCaw)



NIEHS Office of Communications and Public Liaison members, left to right, Ed Kang, Thomas, and Cheryl Thompson, joined scientists and others from throughout the Institute at the talk. (Photo courtesy of Steve McCaw)

# WETP convenes its sixth National Trainers' Exchange

By Ryan Campbell

Nearly 250 trainers from the NIEHS [Worker Education and Training Program \(WETP\)](#) met March 28-29 in Fort Lauderdale, Fla., to improve training methods and exchange ideas on effective health and safety training for emergency response workers. The sixth annual National Trainers' Exchange, titled "Training Today for a Safer Tomorrow," gave trainers an opportunity to discuss new technologies and best practices as well as identify challenges to effective training.



Linked video:

[Learn more about how WETP promotes public health through worker training](#)

(Launches in new window)

Download Media Player: Flash

NIEHS WETP director Chip Hughes welcomed trainers and awardees to the Exchange, and spoke about the vital role of trainers to ensure proper training and convey safety information to workers. Hughes introduced keynote speaker and New York Times best-selling author [Timothy Koegel](#), who instructed trainers on how to make commanding presentations in a training environment. Koegel empowered trainers to engage audiences, learn effective techniques, and use gestures to enhance presentations.

Trainers practiced the recommendations in small groups, to prepare for presentations during the Exchanges' concurrent breakout sessions. The breakout sessions focused on five tracks — advanced training technologies, hazardous waste worker training and emergency response, instructor development, life skills and job training, and training approaches for worker empowerment.

## Emergency response scenarios

The Trainers' Exchange sought to promote regular evaluation of curricula, tools, and instruction, to ensure training experiences maximize learning. An interactive breakout session on tabletop exercises for the Hazardous Waste Operations and Emergency Response Standard (HAZWOPER) training highlighted the importance of effective communication with external response organizations. Gary Yurt, of the non-profit workforce development organization [OAI, Inc.](#), instructed trainers on how to use simulation technology to respond to Hazmat scenarios.



*If attendees were expecting to sit comfortably as Koegel, center, talked about his book, "The Exceptional Presenter," they were in for a surprise when he led them in exercises for engaging training participants. (Photo courtesy of Ted Outwater)*



*Attendee Chip Booth, center, loosened up during an effective gestures exercise led by Koegel. (Photo courtesy of Ted Outwater)*

Highway, rail, and facility accident scenarios sequenced events during a timeframe characterized by complex issues that would challenge communication strategies. Accident simulation training is a useful tool that can reveal gaps and inefficiencies in current response plans.

Mark Catlin, of the [Service Employees International Union \(SEIU\) Education and Support Fund](#), presented a session on instructor development and urged attendees to create and utilize videos in the training environment. In his talk, Catlin emphasized, “Old promotional industry films show effective practices and training challenges.” The U.S. Chemical Safety Board’s video channels, the Mine Safety and Health Administration’s vintage videos, and the Occupational Safety and Health Administration’s training and reference materials library were recommended resources for trainers.

The Exchange focused on several themes to convey key messages to new and veteran trainers — independent trainer innovation is a way to keep training methods current; adoption of new technologies, such as mobile applications, should be merged with traditional training techniques; case studies are valuable training and qualitative tools; and participants have different learning styles and training methods should be adjusted accordingly.

### Roundtable speakers look ahead

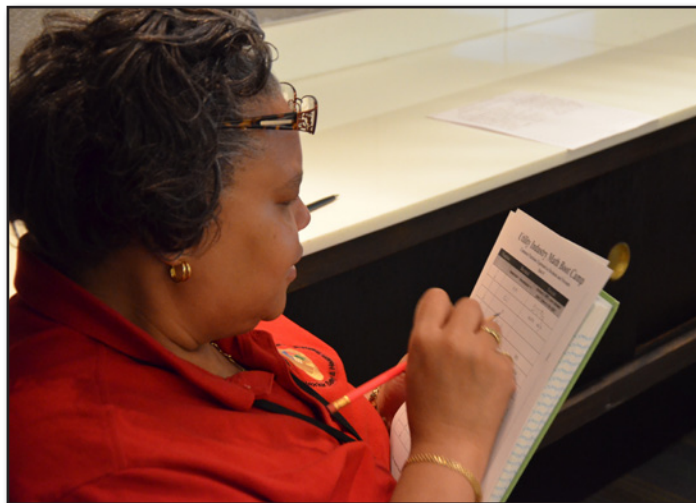
In one of the concluding sessions of the Exchange, the Training Director’s Roundtable brought together five representatives from labor unions, community and environmental justice organizations, and universities, who addressed safe cleanup methods for hazardous waste, to protect public health. Ebony Turner, from the Dillard University Deep South Center for Environmental Justice, discussed the NIEHS Minority Worker Training Program, which provides job training and life skills to individuals who live near hazardous waste sites or in a community near contaminated properties to enable trainees to get jobs that address environmental hazards in their communities.

Panelists also discussed the evolution of their programs and highlighted milestones and early successes. Going forward, the panel recommended partnering with employers and continuing to document success stories that benefit the economy and save lives.

Additional information on the breakout sessions can be found [online](#).



*Kara French, left, of the Center for Construction Research and Training, was the lead presenter for a session on “Teaching Chemical Hazards in the 40-Hour HAZWOPER Class.” (Photo courtesy of Ted Outwater)*



*WETP Industrial Hygienist Sharon Beard joined participants in a workshop session on “Meeting the Need for Higher Level Mathematics in an Increasingly Technical Workforce.” University of Medicine and Dentistry of New Jersey Consortium specialist Allannah Thomas was lead presenter. (Photo courtesy of Ted Outwater)*



*University of Cincinnati Professor Carol Rice, Ph.D., left, a specialist in assessment of industrial exposures, works with fellow attendees during an exercise in a session led by Catlin, “Surgical Masks Are Not Respirators: Training to Abolish a Workplace Myth.” (Photo courtesy of Ted Outwater)*



*WETP Program Analyst Jim Remington made notes about training sessions during a meeting break. The two-day event offered attendees a choice of 56 breakout training sessions on a wide variety of topics. (Photo courtesy of Ted Outwater)*



*Alabama Fire College trainer Ted Kraye led participants in exercises with different types of measurement devices in the “HAZMAT Air Monitoring Exercise.” (Photo courtesy of Ted Outwater)*



*As part of the session on “Use of Dioramas to Enhance Learning Outcomes,” John Hanson, right, of the Lakeshore Technical College/Midwest Consortium, demonstrates how trainers can capitalize on teachable moments with hands-on visualization exercises to represent disaster response scenarios. (Photo courtesy of Ted Outwater)*

(Ryan Campbell is on the staff of MDB, a contractor for the WETP and NIEHS Superfund Research Program.)

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# Team calls for creative approaches to accountability

By Eddy Ball

Librarian Cathy Sarli and bioinformaticist Kristi Holmes, Ph.D., urged scientists and administrators to think outside the citations analysis box to quantify research outcomes and translational impact, during an April 9 presentation at NIEHS.

The Washington University in St. Louis (WUSL) researchers are among several people now thinking divergently about a tracking system framework for evaluating biomedical research — one that includes indicators of impact on public and community health, economic benefit, medical practice, patient outcomes, regulation and legislation, new research directions, and even product development and insurance reimbursement.

Hosted by NIEHS Health Scientist Administrator Kristi Pettibone, Ph.D., who is also involved in high impact tracking for the Institute's Partnerships in Environmental Public Health (PEPH) programs ([see related story](#)), Holmes and Sarli presented the results of ongoing efforts using the [Becker Medical Library Model for Assessment of Research Impact](#). Their model challenges the bibliometric analytical paradigm for accountability long enshrined in tenure/promotion guidelines and grant/program review, with a novel multipronged [guide](#) with more than 80 indicators for metric analysis of biomedical research.

## Beyond the assumption that a high citation count equates with high impact

[Sarli](#), who delivered the first part of the team presentation, referred early in her talk to a statement in the conclusion of a 2007 [commentary](#) by Robert Wells and Judith Whitworth, M.D., on assessing research outcomes. "It is no longer enough to measure what we can," they wrote. "We need to measure what matters."

For people involved in today's biomedical research, Sarli explained, what can be measured easily — frequency of citation — is only a small part of what really matters. And what really matters — the meaningful research outcomes — she added, may be some of the most difficult information to find and quantify.

Spurred by a request in May 2007 by WUSL researcher [Mae Gordon, Ph.D.](#), for assessment of the impact of the Ocular Hypertension Treatment Study (OHTS), the Becker team began looking beyond citations for impact in other areas. Gordon had anecdotal evidence of the OHTS study impact, but she wondered if quantitative, independent indicators were available.



*As she discussed the limitations of citation analysis, Sarli said, "There are so many more ways to tell the story." She and Holmes have developed a hybrid solution with more than 80 indicators, but Sarli cautioned the audience, "I can't give you an SOP — a standard operating procedure." (Photo courtesy of Michael Gaske)*



*"The Becker model is in perpetual beta," Holmes said. "We're always encouraging new input." She pointed to future efforts in what she called ontology extension, — expanding the set of concepts within the research evaluation domain and the relationships between those concepts. (Photo courtesy of Michael Gaske)*

Sarli and Holmes, who joined the effort later on, began the search for novel indicators. Using resources from databases, personal anecdote, organizational guidelines, trade publications, and other so-called grey sources, the team began accumulating evidence that OHTS research had impacted something beyond the world of the PubMed-indexed literary canon, an odyssey they discuss in a 2010 [article](#).

### Challenges for measuring what really matters

In her part of the presentation, [Holmes](#) reinforced Sarli's assessment of the challenges of using the new evaluation paradigm. She conceded it's a messy, time-consuming, and labor-intensive process that is non-linear and non-standardized.

"This is certainly not an exercise for the faint of heart," Holmes told the audience. The supporting documentation may not be publicly available or easily accessible, requiring efforts beyond the standard search. And, it can take creative thinking to establish a direct correlation between the research and the outcomes.

"Researchers need to learn to tell their stories," Holmes said, "be more proactive, and use strategies that enhance their research impact." As budgets tighten and legislators look more critically at funding for scientific research, Holmes predicted, scientists need to demonstrate, clearly, the returns on investment of taxpayer dollars.

Holmes suggested that biomedical researchers begin thinking, at the outset, about potential effects and outcomes in terms of value and benefit beyond publications. She suggested [strategies](#) as simple as using the declarative voice in titles, using names consistently, and writing clearer abstracts with a general, as well as scientific audience, in mind.

Improved dissemination strategies, she added, can include such activities as setting up websites for research output, publishing in open access journals, creating public access repositories for data, taking advantage of social media and outreach opportunities, and tracking the impact of studies according to the kinds of global measures that will resonate with the public and show tangible outcomes in terms of improved health.

#### Citations:

[Sarli CC](#), [Dubinsky EK](#), [Holmes KL](#). 2010. Beyond citation analysis: a model for assessment of research impact. *J Med Libr Assoc* 98(1):17-23.

[Wells R](#), [Whitworth JA](#). 2007. Assessing outcomes of health and medical research: do we measure what counts or count what we can measure? *Aust New Zealand Health Policy* 4:14.

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*As Pettibone, standing, moderated the question and answer session, NIEHS Program Analyst Liam O'Fallon, second from right, asked about measures that might apply to environmental justice and community-based participatory research programs that are part of PEPH. (Photo courtesy of Michael Gaske)*



*In a testimonial posted on the Becker website, Gordon wrote, "Without the thorough analysis recommended by the Becker Model for Assessment of Research Impact, we would have never realized just how far-reaching the impact of our research has been." (Photo courtesy of WUSL)*

# Former NTP counselor named to California EPA post

*By Eddy Ball*

Former NTP advisor Gina Solomon, M.D., will assume a top post with the [California Environmental Protection Agency \(EPA\)](#), according to a California Newswire press release April 11. Solomon served on the NTP Board of Scientific Counselors from July 2008 through June 2011 and, since 1996, she has served as a senior scientist for the Natural Resources Defense Council, an NIEHS Public Interest Partner.

[Solomon](#), who lives in San Francisco, was appointed deputy secretary for science and health at the California EPA by Governor Jerry Brown. Solomon has been the director of the occupational and environmental medicine residency program at the University of California, San Francisco (UCSF) since 2008, and the associate director of the UCSF Pediatric Environmental Health Specialty Unit since 2003.

A strong advocate of environmental public health, Solomon is a longtime friend of NIEHS and a colleague of NIEHS/NTP Director Linda Birnbaum, Ph.D., who applauded the appointment.

“In the past, Gina and I have found ourselves on the same side of the microphone, testifying on the health risks posed by environmental exposures to chemicals,” Birnbaum said. “I think Governor Brown made a great choice when he appointed her to the California EPA, and I have confidence that Gina will do her part to use California’s substantial influence, as what amounts to the world’s eighth largest economy, to help improve public health nationwide.”

The appointment is the latest in a series of public service positions Solomon has held on the state and national levels. She has served on the Scientific Guidance Panel for the California Environmental Contaminant Biomonitoring Program since 2007 and the U.S. Environmental Protection Agency’s Science Advisory Board since 2011. She has also been a member of two committees for the National Academy of Sciences.

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*Solomon is shown above at an NTP Board of Scientific Counselors meeting in 2011. (Photo courtesy of Steve McCaw)*

## PEPH Evaluation Metrics Manual now available

*By Kristi Pettibone*

After more than three years of collaboration, the Partnerships for Environmental Public Health (PEPH) Evaluation Metrics Manual is finally available to the public, free of charge, on the NIEHS PEPH [website](#).

“This manual represents a collective effort to identify and document examples of measures our grantees can use to assess and showcase their work in the community,” said Christie Drew, head of the [Program Analysis Branch \(PAB\)](#) in the NIEHS Division of Extramural Research and Training (DERT). NIEHS program and evaluation staff, grantees, contractors, and other interested parties worked together to develop, review, and revise the manual, to make it user friendly and helpful for a range of stakeholders involved in PEPH programs.

NIEHS has had a long-standing commitment to facilitate and engage community groups in environmental health science research. “You can’t do environmental health without the community,” said NIEHS/ NTP Director Linda Birnbaum, Ph.D., during a forum in March on community-engaged research.

## The PEPH program

In 2008, NIEHS established the PEPH program, to formalize its commitment to outline a coordinated vision for community and academic partnerships. Since then, more than 400 grantees have participated in activities designed to foster networking among grantees within the various NIEHS programs, including webinars and workshops on communicating PEPH findings and translating research to public health policy.

A key principle of the PEPH is community engagement, and NIEHS reached out to the extramural community during the process of re-visioning the program. In response to an NIEHS Request for Information in 2008, the community shared concerns about the lack of evaluation capacity, and the need for tools and approaches to develop project-specific evaluation metrics for public health-related program areas. In response, NIEHS developed the PEPH Evaluation Metrics Manual.

## Evaluation is vital

The PEPH Evaluation Metrics Manual provides ideas about how to measure and document success. It also aims to build a common evaluation language that grantees and program staff can use in discussing PEPH programs. NIEHS will also use the approaches in the manual to evaluate the success of the program as a whole.

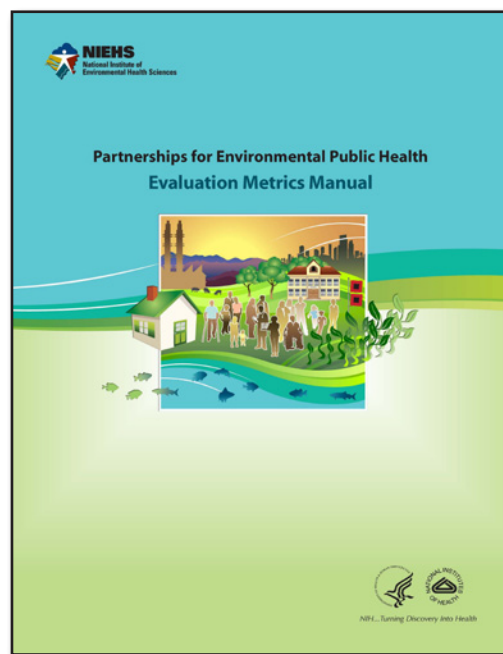
After speaking with more than 50 grantees at training sessions over the last two months, Drew said, “Grantees understand the reasons evaluation is necessary for their programs. They tell us it helps them improve their programs, obtain additional funding, and identify opportunities for new partnerships. They just aren’t sure what they should be evaluating. One of the key messages in our training has been that programs should evaluate those things that are important to them.”

## Development and expected use of the manual

NIEHS developed the manual with significant input from PEPH grantees, program staff, and experts in the field. Drew and her colleagues vetted the manual, at over 30 professional meetings, to more than 250 individuals. Given that this is the most participatory program funded by NIEHS, staff thought it was critical to employ a participatory strategy to develop the tool.



*Drew heads a six-person group of specialists in PAB who provide independent evaluation and analysis of programs within DERT, as well as categorize grants and applications. (Photo courtesy of Steve McCaw)*



*The PEPH manual offers 250 pages of guidance for evaluation of programs ranging from basic research to community-engaged participatory research, outreach and education, and environmental justice.*

NIEHS anticipates that the manual will be a living document and that it will need updating periodically. Opportunities for expansion include new evaluation topics, such as cost-benefit analyses and econometric evaluations, new examples of metrics drawn from the ever-expanding network of PEPH grantees, and new approaches used in programs, such as social media.

NIEHS program staff has been conducting training related to evaluation metrics, and developing stand-alone materials that will be available to the public through the PEPH website and resource center. Staff is also available to conduct webinars related to the PEPH Evaluation Metrics Manual. For more information about the manual and developing metrics, visit [www.niehs.nih.gov/pephmetrics](http://www.niehs.nih.gov/pephmetrics).

Developing the manual was a truly collaborative process and the PAB team offers great thanks to the grantees, community partners, colleagues, and NIEHS staff who contributed.

(Kristi Pettibone, Ph.D., is a health scientist administrator in the NIEHS Program Analysis Branch and a co-author of the new manual.)

## Evaluating PEPH programs

Typical approaches to evaluating research outcomes involve analyzing publications. However, because many PEPH programs do not publish findings related to their community engagement, the team worked with grantees and community members to identify appropriate metrics to demonstrate success in these areas. The manual describes the approach to developing metrics for five crosscutting areas: partnering, leveraging, disseminating findings, training, and capacity building.

Sample metrics from grantee programs include:

- **Demonstrating success at identifying partners** — The University of Cincinnati's anti-idling campaign provided a description of the partners involved and the resources they bring to the project. Cincinnati Public Schools (CPS) provided access to students and schools, Cincinnati Health Department provided nursing services, a Councilwoman provided credibility and the ability to attract attention to the project, and the Hamilton County Department of Environmental Services provided training and information to CPS staff and students.
- **Demonstrating that they communicated their findings in a variety of products** — The Bay Area Breast Cancer and the Environment Research Center described the number and demographics of their social media audience. The center has more than 1,000 followers on twitter and 864 Facebook friends. Followers are 70 percent female and more than half are age 40 or older.
- **Demonstrating the policy impacts of their advocacy** — The Trade, Health, and Environment Impact Project at the University of Southern California documented its contribution to the formation of the San Pedro Bay Ports Clean Air Action Plan. The plan stated that the Ports of Los Angeles and Long Beach would reduce air pollution by 45 percent by 2011. The project also documented its involvement in passing the Clean Air Action Plan, which established a progressive ban on polluting trucks. The plan resulted in a 70 percent reduction in port truck emissions in the Port of Los Angeles in the first year.

# Stem cell fellow moves to UNC

By Robin Arnette

One of the reasons postdocs consistently rank NIEHS as one of the best places to work is the top-notch research training they receive at the Institute. The experience prepares them for a highly competitive job market, as is the case for Raluca Dumitru, M.D., Ph.D., one of the scores of NIEHS postdocs who have landed satisfying careers in the real world.

Dumitru, formally an NIEHS Intramural Research Training Award (IRTA) fellow, has accepted a position as director of the [Human Embryonic Stem Cell Core Facility](#) at the University of North Carolina (UNC) at Chapel Hill. She will help UNC scientists who are interested in using human embryonic stem (ES) cells in their research and will also apply what she's learned over the years to do projects of her own.

“Embryonic stem cells are so unique, because no other cells in the body can differentiate and give rise to all of the cells that comprise a normal embryo,” Dumitru declared. “Studying them allows me to understand normal development and how diseases arise. With my medical background, the subject is perfect for me.”

## Finding her calling

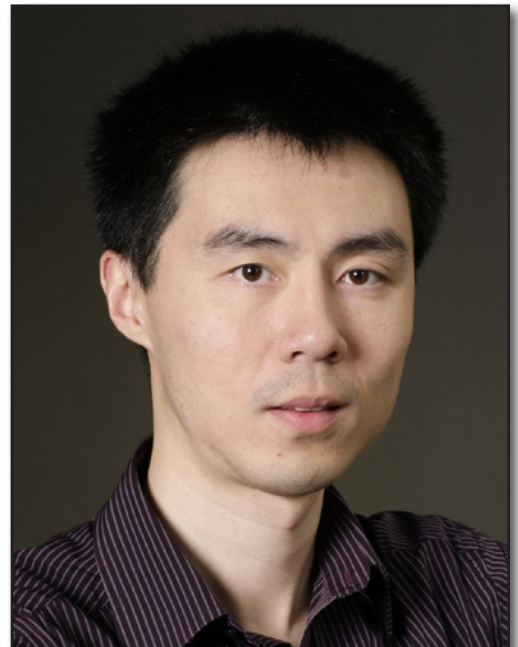
Dumitru finished her medical degree in her native Romania, but when her husband came to the United States to pursue a doctorate in biochemistry, she followed him west. She said she initially planned to study for the medical board exam, but later decided a Ph.D. would give her a different perspective on human illness. She got hooked on research at the University of Nebraska–Lincoln and completed her doctorate there in 2007.

That same year Dumitru began studying the molecular mechanisms of cell death as a postdoc at UNC. Mohanish Deshmukh, Ph.D., served as her advisor, and it was during this stint that she first worked with ES cells. After three years, she joined the NIEHS Stem Cell Biology Group led by [Guang Hu, Ph.D.](#), to get more in-depth training.

Hu said Dumitru exhibited all of the qualities one wants in a researcher — persistence, critical thinking skills, and a willingness to try new things. She studied the Ccr4-Not complex, a newly discovered regulatory complex in human ES cell self-renewal. Dumitru was successful in determining the complex's role in maintaining cell identity between mouse and human ES cells, establishing culture procedures for human ES cells using the latest findings, and building a high-throughput screening platform using human ES cells to study the impact of environmental factors on human development and disease.



*Dumitru said she will bring an extensive knowledge of new ES protocols and reprogramming technology (see text box), learned under Hu's guidance, to her position as director of the UNC Human Embryonic Stem Cell Core Facility. (Photo courtesy of Steve McCaw)*



*Hu said of Dumitru's work on the human ES cell high-throughput screening platform, "It will pioneer the use of these cells in environmental health science studies and open up research directions that were previously inaccessible to environmental scientists." (Photo courtesy of Steve McCaw)*

Hu had no doubt that Dumitru was a superb fit as director of the UNC stem cell core. He said, “Her training and experience will transform the current facility and greatly accelerate its research using human stem cells.”

In addition to being a wife and researcher, Dumitru is also the mother of a seven-year-old son. She said she spends as much time with him as she can after work and especially on the weekends. When asked how she is able to balance it all, she said it helps to have a supportive spouse and to know where your priorities lie.

“The most important thing to me is being a mom,” Dumitru added, “but when you love the work you do, you find ways to weave all of your responsibilities together.”

## Reprogramming cells

Dumitru said a Japanese group first reprogrammed human skin fibroblast cells into stem cells in 2007. Members of the team were able to transform the skin cells, by introducing four specific transcription factors that were critical for reverting these somatic or body cells back to an undifferentiated state. Dumitru believes the technology may offer a viable treatment option for people suffering from a variety of conditions, for example, neurodegenerative disease.

“You could take the patient’s skin fibroblasts, introduce those transcription factors, and differentiate the cells into neurons,” Dumitru explained. “Theoretically, you could transplant those neurons. This research is in its infancy, but I think it has huge potential.”

Dumitru is an author on a new paper from the Hu group featured as an Intramural paper of the month ([see summary](#)).

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## Facebook and Twitter drive NIEHS social media expansion

*By Ian Thomas*

With many Americans now turning to such services as Facebook and Twitter for the bulk of their news and information, NIEHS continues to expand the reach of its environmental health message by adapting it for the ever-exploding world of social media.

“People throughout the world are realizing that their health is linked to their environment and they want more information about this connection,” said Christine Flowers, director of the NIEHS Office of Communications and Public Liaison (OCPL). “So, we’re taking our research results to the public in a way that’s easy to understand and also easy to access. Social media is simply where people go for information. We need to be there, ensuring that accurate and reliable information is available.”

Since the launch of its [Twitter page](#) in December 2010, NIEHS has accumulated more than 3,100 followers, while its [Facebook page](#), launched in December 2011, currently draws more than 4,000 visits per week.



*Since her arrival to NIEHS in 2004, Flowers has expanded OCPL’s informational suite to include new mediums such as social media and [YouTube](#), in addition to conventional news services such as [press releases](#), [fact sheets](#), and a monthly newsletter. (Photo courtesy Steve McCaw)*

“When people wake up in the morning, they’re not reading the local paper for the news or even going to their favorite website,” said Ed Kang, a public affairs specialist for OCPL and a social media aficionado. “They’re checking their Facebook pages and Twitter feeds to see what’s going on in the world. Therefore, as content generators, we have to have information ready for them to find when they get there.”

### Getting to the point

One of the things that make social media so appealing is its abbreviated format. In the case of Twitter, user posts, referred to as tweets, may not exceed 140 characters. That puts pressure on communicators to write content that is both enticing to the reader and also concise.

“In today’s world of information, we only get a few seconds to capture someone’s attention with our message,” Kang noted.

Another upside to social media is the ability of its content to go viral through posting and reposting by direct and secondary followers.

“Direct followers are a great metric for measuring our reach, but it’s those secondary followers that show us the true potential of our efforts,” Kang explained. “Those who follow us directly are always looking for our content, but it’s the people who follow them, the ones who only get our information through second-hand “like” and retweet features, that we want to connect with.”

At present, NIEHS has more than 700,000 secondary followers on Twitter.

### A future on the go

As sales of smartphones, tablets, e-readers, and portable information devices continue to skyrocket, thus making mobile app content and social media infinitely more accessible to users, Kang is adamant that NIEHS must tailor both its message and its delivery methods to evolve with the times.

“Every day the American public is inundated with news stories about various diseases, cancer-causing agents, and countless other topics that leave them asking questions, and we can’t expect them to simply seek out our website for the answers,” said Kang. “Through social media, however, we can put that information right in front of them, so our latest research is just a hashtag away.”

(Ian Thomas is a public affairs specialist with the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

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*Kang points out that social media also provides a number of benefits to NIEHS personnel, such as employee news, schedules, and event information, plus a wealth of opportunities for research publicity. (Photo courtesy Steve McCaw)*

# Former NIEHS fellow receives travel award

By Robin Arnette

Quiana Childress intends to be a physician one day, but relishes the thought of doing biomedical research just as much as caring for patients. Childress, a former NIEHS fellow, was selected to receive a Federation of American Societies for Experimental Biology Minority Access to Research Careers travel award to attend the [Experimental Biology 2012 meeting](#) April 21-25 in San Diego. She joined the nearly 14,000 other scientists and exhibitors at the multidisciplinary conference that covered fields as diverse as anatomy, physiology, biochemistry, pathology, nutrition, and pharmacology.

Childress is currently at Meharry Medical College in Nashville, Tenn., participating in the post-baccalaureate program, which provides students from disadvantaged backgrounds with the skills they need to successfully graduate from health profession schools. When she isn't studying for classes, she investigates vascular signaling under the guidance of her faculty advisor [Evangeline Motley-Johnson, Ph.D.](#), who is also associate dean of the School of Graduate Studies and Research at Meharry.

Motley-Johnson's laboratory examines protease-activated receptor signaling in endothelial cells, or the cells that line the inner layer of blood vessels, and how this signaling regulates nitric oxide production. Her lab presented its current findings at the meeting.

When asked why her research is important, Childress said, "Endothelial dysfunction is a major contributor to hypertension. I would like to understand the signaling pathways involved in this disease so that therapeutic agents can be developed at the molecular level."

Motley-Johnson has mentored several graduate students and knows the importance of students attending national conferences. She said these gatherings offer invaluable career development opportunities for students, everything from networking with seasoned scientists to learning about the latest research through seminars and poster sessions. Motley-Johnson was thrilled that Childress had a chance to polish her scientific skills by participating in the meeting.

"Quiana will be able to build on her knowledge base," Motley-Johnson said, "which will help her focus her career goals."

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*While at NIEHS, Childress worked with Clinical Research Unit medical director and Laboratory of Respiratory Biology researcher Stavros Garantziotis, M.D. They studied a protein that may have a role in the tissue rejection that some lung transplant patients face. (Photo courtesy of Craffe Eye Photography)*

## Doctor, researcher, survivor

Childress believes when she eventually becomes a physician, her research experience will greatly benefit her patients by helping her understand disease in a fundamental way. Although she hasn't attained her goal yet, her past triumphs leave little doubt that she will complete her mission ([see story](#)).

## Folt appointed interim president at Dartmouth

[Carol Folt, Ph.D.](#), a member of the Superfund Research Program team at Dartmouth College since it started in 1995, was appointed interim president of the college April 17, following the election of President [Jim Yong Kim, M.D., Ph.D.](#), to lead the World Bank.



Folt's areas of expertise include ecotoxicology, health-environment interactions, and science education. Metal toxicity and the effects of dietary mercury and arsenic on aquatic life and human health is her research focus. She and her colleagues developed new technologies to assess mercury environmental exposure and its effects. They also conduct crosscutting research on chemical signaling, restoration and conservation of Atlantic salmon, and global climate change.

Folt serves on federal scientific review panels and foundation boards, reviews for journals, and has held elected offices in international scientific societies. She became a fellow of the American Association for the Advancement of Sciences in recognition of her contributions to environmental science and higher education.

A faculty member since 1983, Folt was named Provost in May 2010, which made her the second ranking officer at Dartmouth. Folt received a B.A. in aquatic biology and an M.A. in biology from the University of California, Santa Barbara; earned a Ph.D. from the University of California, Davis; and completed a postdoctoral fellow at the W.K. Kellogg Biological Station.

A [press release](#) about Folt's appointment is available online through the Dartmouth College Office of Public Affairs.

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*Dartmouth College Interim President Carol Folt. (Photo courtesy of Rob Bossi and Dartmouth College)*

## Trainees reach out to area students for NC DNA Day

*By Jeffrey Stumpf*

This April, NIEHS trainees once again traded in their pipettes for hall passes to participate in [North Carolina DNA Day](#). Commemorating the completion of the Human Genome Project in April 2003 and the anniversary of the discovery of DNA's double helix by Watson and Crick in 1953, DNA Day sends scientists to North Carolina high schools to educate students about DNA-related topics, as well as exciting career opportunities in science and biotechnology.

The University of North Carolina (UNC) at Chapel Hill hosts the statewide program that puts exciting topics, such as forensics and genetic diseases, into the classroom. Except for UNC itself, NIEHS sent more scientists out to area high schools than any other participating institution.

### Scientific substance and role models for students

In addition to teaching students about modern molecular biology, DNA Day encourages scientists to talk about what excites them in biology. John House, Ph.D., an NIEHS trainee, relayed his enthusiasm for science. “I wanted high school students to have a chance to meet a scientist and hear about science and our passion for research,” he said.

Fellow NIEHS Trainee, April Binder, Ph.D., agreed, “NC DNA Day is a great way to bring the fun and excitement of science into the community, and share what we do every day with students from diverse backgrounds.”

Postdoctoral researcher Sarah Swerdlow, Ph.D., challenged the students’ misconception of what a scientist looks like by asking them rhetorically, “Do I look like an old man in a white coat?” Binder also eased the minds of the fashion-concerned students. “Most students were shocked to hear that I don’t wear a white lab coat all of the time.” Binder recalled.

### Science leaves some students with a bitter taste in their mouths

Some trainees used the example of cystic fibrosis to teach students how different traits are expressed and what can cause a genetic disease. The class was accompanied by a hands-on activity using patient samples and DNA sequences to determine which patient has cystic fibrosis. The link from DNA to genetic disease, according to House, stimulated the students’ interests. “The students were most interested in how a mutation caused cystic fibrosis and how we might one day cure the disease with gene therapy,” he said.

Other trainees allowed students to sample phenylthiocarbamide (PTC) chemical paper to determine if they could taste the bitter chemical. Tasting PTC depends on the composition of the PTC gene, which encodes a bitter taste receptor protein. NIEHS trainee Sarah Swerdlow noticed that the variety of the students’ responses made the activity fun.

“They enjoyed watching their classmates’ faces,” Swerdlow observed. “Some of them needed a sucker to get the taste out of their mouths.”

Fortunately, a sucker was part of the next activity. Using the dye of the sucker, students were able to count papillae on their tongue and determine whether those with sensitive tastes have more papillae. While the results of their experiment may have varied from what was expected, Swerdlow introduced the unexpected data as a real science lesson. “I think it is a good lesson that results are not always perfect,” Swerdlow noted. “Unexpected results are a part of biology.”



*House performs research in the Genetics, Environment, and Respiratory Disease Group at NIEHS. (Photo courtesy of Steve McCaw)*



*Swerdlow studies mutagenesis in *E. coli* in the NIEHS Laboratory of Molecular Genetics. (Photo courtesy of Steve McCaw)*



*Binder is a postdoctoral trainee in the Laboratory of Reproductive and Developmental Toxicology and a veteran DNA Day ambassador. (Photo courtesy of Steve McCaw)*

The students also performed some hands-on activities that included extracting DNA from saliva, and filled out a genetic wheel — an exercise that diagrammed their genetic diversity. These activities taught about the basic functions of DNA and the molecular tools that are used to study it. But, in the end, Binder noted that the students were most interested in science that is most accessible to them.

“The students asked great thought-provoking questions, especially about DNA and forensics, because they see and hear so much about it on TV these days,” said Binder.

(Jeffrey Stumpf, Ph.D., is a research fellow in the NIEHS Laboratory of Molecular Genetics Mitochondrial DNA Replication Group, who also participated in DNA Day as a DNA ambassador.)

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## Birnbaum discusses 12th RoC at congressional joint hearing

*By Ian Thomas*

NIEHS/NTP Director Linda Birnbaum, Ph.D., addressed questions regarding NTP’s [12th Report on Carcinogens \(RoC\)](#) April 24 during a U.S. House of Representatives joint subcommittee hearing. Testifying in front of the Committee on Science, Space, and Technology, Subcommittee on Investigations and Oversight, as well as the Committee on Small Business, Subcommittee on Healthcare and Technology, Birnbaum addressed a wide range of questions regarding the RoC’s contents, and the rigorous peer review process by which scientific research and public feedback are used during its compilation.

“The RoC is a science-based, public health document that provides information about the relationship between the environment and cancer,” explained Birnbaum. “The Report lists a wide range of substances, including metals, pesticides, drugs, natural and synthetic chemicals, and biological agents that are considered cancer hazards for people in the U.S.”

Launched in 1978 as part of the Public Health Services Act, the RoC takes into account a number of different factors when determining a substance’s potential hazard for cancer. These include such things as the amount and duration of exposure, as well as an individual’s susceptibility to a substance. Still, Birnbaum was quick to point out that the RoC is not a tool for risk assessment.

“This is not a regulatory document,” she noted. “However, the RoC does provide decision makers and the public with information they can use to make decisions about exposures to cancer-causing substances.”



*Birnbaum was accompanied to the hearing by members of the NIEHS staff located in Bethesda, Md. (Photo courtesy of Steve McCaw)*

## **A pair of categories**

The RoC lists substances in one of two categories, “known to be carcinogens” and “reasonably anticipated to be carcinogens.”

For a substance to be listed in the known category, there must be sufficient evidence from human studies that indicates a causal relationship between exposure to the substance and human cancer. For a substance to be classified in the reasonably anticipated category, it must fit one of three scenarios: limited evidence it causes cancer from studies in humans; sufficient evidence it causes cancer from studies in animals; or evidence that the substance is a member of a class of substances already listed in the Report or that it causes biological effects known to lead to the development of cancer in humans. “The decision to list a substance in the RoC is based on scientific judgment, with consideration of all relevant research data and input from both advisory groups and the public,” said Birnbaum.

## **Involving the public**

While the preparation of each edition of the RoC involves a multi-step process, including expert advisory reviews, independent external peer reviews, and outside input from agencies, such as the U.S. Food and Drug Administration, U.S. Environmental Protection Agency, and Consumer Product Safety Commission, among others, Birnbaum added that anyone can nominate a substance for listing or removal from the Report, be it a field-leading scientist or a private citizen.

“In the case of the 12th RoC, we actually increased the number of opportunities for public review and input,” said Birnbaum, adding that public comments were solicited on six different occasions.

## **Looking ahead**

As NTP moves forward on the 13th RoC, Birnbaum and her staff have revised the process for preparation of the report with regard to the transparency and efficiency, while continuing to maintain the rigorous investigative standards for which the document has long been known.

“We believe the RoC is, and will remain, an important public health document, because it empowers the public and decision makers with the information they need to make informed choices about potentially cancer-causing substances and hazards,” said Birnbaum. “However, a process like this can never be too thorough, which is why it’s vital for us, as researchers, to always be mindful of new ways to improve it.”

(Ian Thomas is a public affairs specialist for the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

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# **Environmental justice advocates honored as green champions**

*By Ian Thomas*

NIEHS staffers Chip Hughes, Sharon Beard, and Liam O’Fallon are being honored with the Good Neighbor Award by the U.S. Department of Health and Human Services (HHS), as part of its annual Green Champions Awards. Recognizing outstanding achievement at the local level, the Good Neighbor Award salutes those HHS employees, groups, and organizations that coordinate with community partners and stakeholders to educate the public on the importance of a healthy environment.

“It truly is an honor to receive this award,” said Hughes, who is the director of the NIEHS [Worker Education and Training Program \(WETP\)](#). “Ultimately, our success with issues like environmental justice will hinge on our ability to show people how their health is tied to their environment. For us, that starts right here in the Triangle [Research Triangle Park area].”

Comprised of several individual and group categories, the Green Champion Awards acknowledge outstanding achievement in a wide range of environmental health issues. These include environmental stewardship, corporate responsibility, and environmental justice, among others.

“So many people that we work with are at an increased risk for disease and illness, because they work in the dirtiest jobs,” said Beard, an industrial hygienist and program administrator with WETP. “By working together with our partners at HHS, and here at home, we’re able to help them live healthier lives, by giving them the tools and education they need to do those jobs as safely as possible.”

Liam O’Fallon, a program analyst with NIEHS Division of Extramural Research and Training [Community Outreach and Engagement Program](#) agrees.

“Issues like environmental justice and climate change affect all of us, and people genuinely want to know how they can help out,” said O’Fallon. “That’s what makes our job such a thrill, because we get to go out, into their homes and workplaces, and show them how to do just that, by making changes to the environments around them.”

Hughes, Beard, and O’Fallon were joined on their team by representatives from other HHS agencies, including the National Institute for Occupational Safety and Health, the Office of the Assistant Secretary for Health, and the Centers for Disease Control and Prevention. Much of their work can be found in the [2012 HHS Environmental Justice Strategy and Implementation Plan](#), an agency-wide effort to reduce health disparities among minority and low-income workers, through increased education and worker training opportunities.

To learn more about the HHS Green Champion Awards, or for a complete list of winners and nominees, visit the [HHS website](#).

(Ian Thomas is a public affairs specialist with the NIEHS Office of Communications and Public Liaison, and a regular contributor to the Environmental Factor.)

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*Good Neighbor Award winners, shown left to right, O’Fallon, Beard, and Hughes. (Photo courtesy of Steve McCaw)*

# Science Notebook

## Keith Yamamoto delivers 2012 Rodbell Lecture


By Brant Hamel

Keith Yamamoto, Ph.D., continued an annual tradition of outstanding Rodbell lectures with his seminar April 10, titled “Cell-, Gene-, and Physiology-Specific Regulation by the Glucocorticoid Receptor.” Yamamoto’s talk explored the specificity of transcriptional regulation by the glucocorticoid receptor (GR), which he explained integrates signals from multiple contexts to direct its regulation of gene expression.

**Yamamoto** is the vice chancellor for research, executive vice dean of the school of medicine, and a professor of cellular and molecular pharmacology at the University of California, San Francisco (UCSF), who has published more than 150 articles greatly increasing the understanding of nuclear receptor structure and function. Just as importantly, Yamamoto is very involved in improving the scientific enterprise through his service on multiple committees exploring science training and education, scientific policy, and the peer review process at NIH.





Keith Yamamoto, Ph.D., delivered the 14th annual Dr. Martin Rodbell Lecture Series at NIEHS, with a talk focusing on the regulation of the GR function. He is a member of the National Academy of Sciences and the Institute of Medicine, and a fellow of the American Association for the Advancement of Science. (Photo courtesy of Michael Garske)



**Linked video:**  
[Watch as Yamamoto describes his vision of the future of science at UCSF \(04:23\)](#)

(Launches in new window)

Download Media Player:  Flash 

### Multiple levels of signals converge to determine GR signaling

The GR is a member of the nuclear receptor family of transcription factors, which binds to steroids to regulate many physiological processes ranging from glucose signaling to the anti-inflammatory response. A key enigma is that the GR is highly variable in how it regulates gene expression in different types of cells. Yamamoto explained this, in large part, is due to the complexity of the macromolecular complex that it organizes, which may contain up to 100 different polypeptides that vary from cell to cell and gene to gene.



As she has with every lecture in the Rodbell series, Barbara Rodbell was on hand for Yamamoto’s talk. Her late husband, Martin Rodbell, Ph.D., a 1994 Nobel Prize winner and former NIEHS scientific director, delivered the inaugural Dr. Martin Rodbell Lecture Series seminar in 1998, just weeks before his death. (Photo courtesy of Steve McCaw)

Yamamoto detailed how signals converge on the receptor from multiple levels, including gene-specific sequences provided by the sequence of the GR-DNA binding site; cell-specific signals, such as the identity of coregulators expressed in a given cell; and physiological signals, including those that result in post-translational modifications of the receptor. He explained that instead of thinking of the receptor as having a specific intrinsic activity, it is more appropriate to think of it as a signal integrator that results in a receptor complex with different activities that are highly dependent upon gene, cell, and physiological context.

### Regulatory logic circuits allow complex gene activation patterns

To better understand the mechanism of cell-specific regulation by the GR, Yamamoto searched for genes that were induced in one cell type, but repressed in another, in response to glucocorticoid treatment. One of the genes discovered, ANKRD1, displayed an intriguing kinetic profile in osteosarcoma cells of a very brief activation followed by a prolonged repression. Yamamoto found that ANKRD1 and 29 other genes all followed a logic circuit known as an incoherent feed-forward loop type I, in which the initial activation of gene expression is quenched after a gene-specific inhibitory threshold is reached. He is now searching for the mechanism that results in this kinetic profile in certain cell types, but not others.

### DNA is an allosteric effector of GR

Although it has long been known that the binding of varying ligands results in differing conformational changes of the GR, Yamamoto provided the unexpected finding that DNA itself can act allosterically to alter the structure of the receptor. Using X-ray crystallography, Yamamoto solved the structure of the DNA binding domain of the GR bound to a variety of different DNA sequences. Even alterations in bases that do not directly contact the receptor were found to lead to structural changes in the receptor that might be expected to alter its activity or bind to other co-regulatory proteins. Yamamoto was not content to stop at the static pictures provided by crystallography and expanded the study through the use of nuclear magnetic resonance spectroscopy, to show that the shifts induced by DNA binding follow an allosteric path that extends all the way to the dimerization interface. Conversely, mutation of the dimerization interface leads to alterations in DNA binding capability through the same allosteric pathway working in reverse.

Yamamoto's talk was co-hosted by NIEHS Laboratory of Molecular Carcinogenesis head [Trevor Archer, Ph.D.](#), who introduced the speaker and moderated the question and answer session, and NIEHS Laboratory of Signal Transduction head [John Cidlowski, Ph.D.](#)



*Yamamoto's lecture brought out a standing-room-only crowd to hear his insights into GR signaling. Shown above, left to right, are NIEHS biologist Esther Hou, research fellow Mallikarjuna Metukuri, Ph.D., and postdoctoral fellow Sabrina Robertson, Ph.D. (Photo courtesy of Michael Garske)*



*Yamamoto was presented with the Rodbell statue, to honor his contributions to the understanding of nuclear receptor function and his selection as the 2012 Rodbell lecturer. (Photo courtesy of Steve McCaw)*



*Carl Regutti, center, the sculptor who crafted the Rodbell statue from Martin Rodbell's hand, attended his first Rodbell lecture since hearing Rodbell speak 14 years ago. (Photo courtesy of Michael Garske)*

*Yamamoto explained that it is the integration of multiple signals by the GR that results in its ability to stimulate transcription in a given context. (Photo courtesy of Michael Garske)*

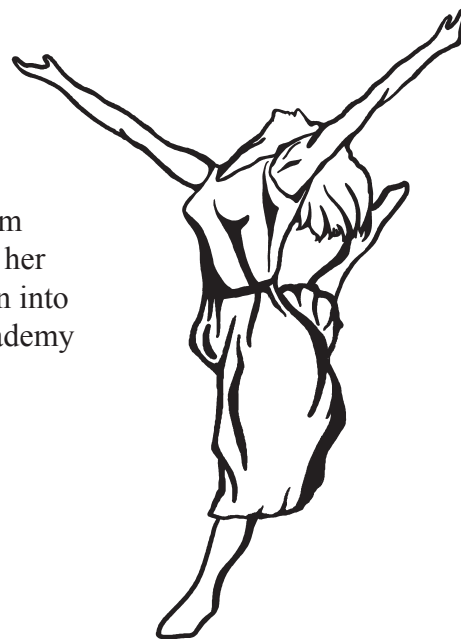
(Brant Hamel, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Laboratory of Signal Transduction.)

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## Spirit Lecture honors accomplished female scientist Gail Martin

*By Ashley Godfrey*

In recognition of Women's History Month, University of California, San Francisco (UCSF) Professor of Anatomy Gail Martin, Ph.D., visited NIEHS April 16 to deliver the 2012 NIEHS Spirit Lecture, co-sponsored by the Diversity Council and Women Scientists Assembly. This annual event, now in its 11th year, recognizes outstanding women who have made significant contributions to their scientific field. In her talk, "From Stem Cells to Complex Patterning in the Embryo," Martin gave a retrospective of her career, which has consisted of many notable achievements including election into both the American Academy of Arts and Sciences and the U.S. National Academy of Sciences.





*The Spirit Lecture logo depicts the striving for self-fulfillment the series celebrates each year.*



**Linked video:**

Watch 'Women in History,' a slide show created for the Spirit Lecture series by NTP scientist Brad Collins (07:17)

(Launches in new window)

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## Paving the way for future research

In his introduction Deputy Director Rick Woychik, Ph.D. explained, "[Martin's] research has had a profound impact on many members of the biomedical community." In her early work, Martin was able to create a reproducible method for maintaining embryonic carcinoma (EC) cells in their pluripotent, or undifferentiated, state in culture. These cells are derived from a specific type of tumor and are unique in their ability to give rise to many different cell types.

Continuing this line of work, Martin became one of the first scientists to find that these pluripotent cells could be directly collected from embryos and used in the lab as a model system to study normal embryo development. Martin's breakthrough introduced the scientific world to embryonic stem cells and helped to kick start the research of this continuously growing biomedical field.

Later on in her career, Martin became interested in studying the genes that pattern the normal embryo and began an extensive body of work on the fibroblast growth factor (FGF) family of proteins. These proteins are key players in the process of proliferation and differentiation in a wide variety of cells and tissues. Her research has established a model, which suggests that the levels of FGF signaling during development can explain how complex patterning of different tissues and organs is accomplished.

Martin's research has also led to the discovery of a set of genes whose job is to turn down FGF signaling during development, the sprouty gene family. Expression of these genes is induced by FGF signaling and leads to an exquisite negative feedback loop that keeps FGF signaling in check by expression of the sprouty genes.

"We have found that in many tissues that sprouty genes are there to prevent cells from doing something they are capable of doing, but shouldn't do for normal development," Martin told the audience.

## Perseverance pays off in the end

When asked about her advice to young women scientists, Martin's answer demonstrated that her hard work and determination were key factors in her own success. She further explained that her own career path did not always follow an easy road. For example, when she was a postdoctoral student in London, she was not allowed to work in the same institute as her husband because it was considered nepotism, but she was able to find a position in a different area.



*Martin's introduction emphasized that her lecture was more than just a retrospective about her career, but was really about the people who worked with her. Throughout her talk Martin made sure to point out the scientists who have worked in her lab and how their contributions helped to guide their own successful careers. Martin was proud to point out that two of these scientists, [Terry Magnuson, Ph.D.](#), and [Alex Joyner, Ph.D.](#), have recently been inducted into the American Academy of Arts and Sciences. (Photo courtesy of Steve McCaw)*



*Woychik explained how Martin was not only an exceptional scientist, but that her efforts to build central databases in order to keep important scientific discoveries connected across different labs has redefined collaborative activities at her university. (Photo courtesy of Steve McCaw)*

Following her early success, Martin said, “I was able to talk my way into a faculty position [at UCSF].” This position however, was not a tenure track position, which meant she had no extra salary, no start-up package, and no real job security. This of course did not discourage Martin, who successfully kept her lab going for 10 years before UCSF finally made her a full professor in 1985.

“I was able to take a back route in, but it was tough,” stated Martin. She emphasized that she could not have been so successful without the help and support of others and said she considers herself really blessed by the young scientists who she has had the opportunity to mentor.

Martin concluded her lecture by stating that she was planning to retire and leave her work for the next generation of scientists.

A reception followed Martin’s talk, with reception provided by donations from members of the Spirit Lecture Committee.

(Ashley Godfrey, Ph.D. is a postdoctoral fellow in the Molecular and Genetic Epidemiology Group in the NIEHS Laboratory of Molecular Carcinogenesis).



*Martin’s lecture was well attended by many members of the NIEHS community. Shown, left to right, are Charlie Tate, Jan Drake, Ph.D., former Laboratory of Molecular Genetics chief, and Jerry Heindel, Ph.D., Division of Extramural Research and Training program administrator. (Photo courtesy of Steve McCaw)*



*Several attendees joined Martin for a look at a picture of her son as a baby along with his karotype, a representation of his chromosomal structure. Shown, left to right, are Angela King-Herbert, D.V.M., Veronica Robinson, Helen Cunny, Ph.D., Martin, Spirit Lecture Committee chair Molly Vallant, Diane Spencer, and Grace Kissling, Ph.D. (Photo courtesy of Steve McCaw)*



*Woychik, left, joined members of the Spirit Lecture Committee and on the patio during the reception. Shown, left to right, are Kissling, Eli Ney, Diversity Council chair Brad Collins, Spencer, Martin, Vallant, King-Herbert, and Robinson. (Photo courtesy of Steve McCaw)*

# NIEHS scientist wins top rating at cancer conference

By Heather King

NIEHS Staff Scientist [Harriet Kinyamu, Ph.D.](#), won a poster prize at the American Association for Cancer Research (AACR) annual meeting March 31-April 4 in Chicago. Kinyamu, who works in the Laboratory of Molecular Carcinogenesis (LMC), presented a poster describing her research on the RNA-binding protein LIN28.

The poster was designated top ranked by the [AACR](#) with a special listing in the itinerary planner and a ribbon to signify its status during the poster session. Kinyamu said she was elated to be recognized for her work, and was quick to thank her supervisor, LMC head Trevor Archer, Ph. D., and NIEHS biologist Jun Yang for their contributions.

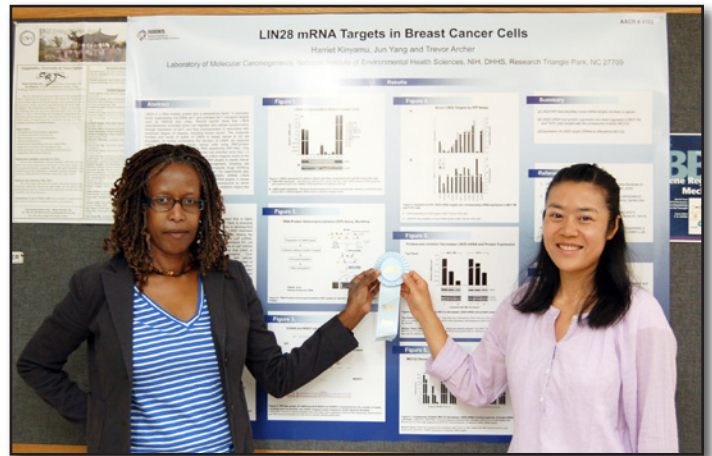
The AACR seeks to prevent and cure cancer through research and education, and its mission is well aligned to the goals of the LMC, which seeks to improve cancer prevention and therapy by investigating biological events that lead to cancer. Archer served as a chairperson and organizer for the AACR meeting, heading The Ruth Sager Memorial Symposium on Cancer Genetics and Epigenetics.

Archer also presented work by Kevin Trotter and Ajeet Singh, Ph.D., that demonstrates the role of chromatin remodeling proteins in transcription and development. Several other LMC members attended the AACR meeting along with Archer and Kinyamu, including head of the Molecular and Genetic Epidemiology Group Jack Taylor, M.D., Ph.D., and postdoctoral fellows Kimberly Wiggins, Ph.D., Ashley Godfrey, Ph.D., and Jill Hesse, Ph.D. (see text box)

## Targeting protein misregulation

When asked about the relationship between her work with LIN28 and cancer, Kinyamu explained, “There is some belief that important molecules in development are misregulated in cancer. The LIN28 protein is a classic example of this.”

Kinyamu’s research has identified interactions between LIN28 and specific RNA transcripts that allow LIN28 to regulate gene expression during



Kinyamu, left, and Yang held their prize ribbon in front of their winning poster. (Photo courtesy of Heather King)

## Presentations by NIEHS researchers at the AACR meeting

### Talk —

- [Chromatin remodeling proteins in transcription and development](#), Trevor Archer, Ph.D., Kevin Trotter, Ajeet Singh, Ph.D.

### Posters —

- LIN28 mRNA targets in breast cancer cells, Harriet Kinyamu, Jun Yang, Archer.
- [Inhibition of the ubiquitin proteasome system differentially regulates glucocorticoid receptor-mediated transcriptional processes](#), Kimberly Wiggins, Ph.D., Valerie Davis, Ph.D., Dhiral Phadke, Ruchir Shah, Archer.
- [Serum miRNAs as an early marker for breast cancer](#), Ashley Godfrey, Ph.D., Zongli Xu, Ph.D., Clarice Weinberg, Ph.D., Paul Wade, Ph.D., Lisa DeRoo, Ph.D., Dale Sandler, Ph.D., Jack Taylor, M.D., Ph.D.
- [Genome-wide small RNA sequencing and gene expression analysis reveals a microRNA profile reflective of cancer-susceptibility in ATM deficient human mammary epithelial cells](#), Jill Hesse, Ph.D., Cynthia Innes, Liwen Liu, Richard Paules, Ph.D.

development and also allow it to play a role in tumorigenesis. Her poster also described experiments that show MG132, a compound similar to the chemotherapeutic Velcade, inhibits LIN28 activity.

A supportive research environment is something Kinyamu feels has been essential to her work, and to work conducted throughout LMC, where scientists are constantly working to better define biological mechanisms that are important during carcinogenesis. In the LMC, intrepid science is not only encouraged, but also supported with mentorship and resources. Kinyamu noted, in particular, the ability to use new technology to answer scientific questions as instrumental in her own work.

New sequencing technologies have given researchers, such as Kinyamu, the ability to analyze global changes in gene expression and protein promoter interactions. Access to such technology comes with working in a program poised on the cutting edge of scientific discovery and of new experimental methods. Kinyamu's AACR poster award reflects a winning combination of experimental freedom, supportive mentorship, and talented team members — what she considers hallmarks of the NIEHS Intramural research program.

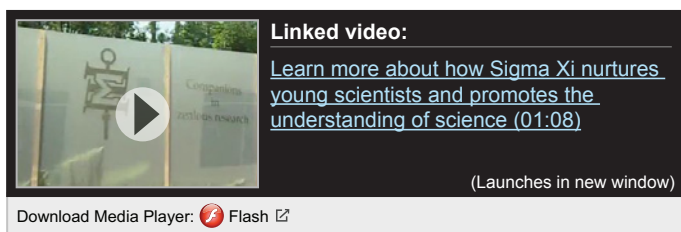
(Heather King, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Laboratory of Structural Biology Protein Expression Core.)

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## Science writers learn about NIEHS nano program

*By Heather King*

NIEHS Health Scientist Administrator Sri Nadadur, Ph.D., delivered the American Scientist's lunchtime seminar March 27 at Sigma Xi headquarters in Research Triangle Park (RTP), N.C. This monthly [seminar series](#) brings research scientists together with an audience of science writers and other scientific communications professionals.



In this forum, scientists have an opportunity to consider the broader implications of their work, while science writers and communicators have a chance to hear firsthand about current research efforts and new findings. In his presentation, Nadadur spoke about the potential health risks associated with environmental exposure to some engineered nanomaterials (ENMs), and the role of NIEHS in establishing a program to investigate those risks and their public health implications.

*Nadadur was animated as he talked about the variables in host susceptibility, material characteristics, and analysis that have made it difficult to reach definitive conclusions about the health effects of exposure to ENMs. (Photo courtesy of Steve McCaw)*

## Focus on health concerns

Nadadur began his talk, “Nanotechnology Environmental Health and Safety Research at NIEHS,” by describing the increasing use of ENMs in such consumer products as sunscreen, cosmetics, food, and pharmaceuticals. “There may be potential health concerns related to ENMs, substances used in abundance in many new products, but not yet well characterized in terms of their bioactivity,” he explained.

A coalition of government agencies is currently studying ENMs as part of the National Nanotechnology Initiative. NIEHS is playing a key role in this initiative by supporting research to gain fundamental understanding of ENM interactions with biology and ultimately their potential health effects. One of the initial activities in this direction is identifying reliable and reproducible test systems.

Nadadur emphasized the challenges of relating specific ENM biophysical characteristics to adverse effects on human health. Response to ENM exposure can be highly variable, and the toxicity of a particular ENM often varies, based on the individual, tissue, or cell type exposed. Additionally, the manufacturing process can lead to subtle differences in surface area, contaminants, or other ENM qualities, further complicating the dose-response relationship.

To illustrate, Nadadur pointed to several conflicting studies of the association between carbon nanotube exposure and lung damage similar to that observed in asbestos-related injuries. Carbon nanotubes are prized for their strength and used in a range of products from electronics to automotive components. Though some carbon nanotubes are harmful, others are not, and understanding why, based on key physical properties, is the major goal of the NIEHS program.

In addition to concerns about carbon nanotubes, Nadadur said there are issues arising from the increasing use of cerium oxide (CeO<sub>2</sub>) nanoparticles as a diesel additive to increase engine efficiency. Exposure to macroscale CeO<sub>2</sub> is associated with liver damage, but it also reduces combustion-related pollution and possesses antioxidant properties. However, little is known regarding the health and safety of nanoscale CeO<sub>2</sub> particles found in exhaust emissions. According to Nadadur, more research into the costs, benefits, and human health effects of CeO<sub>2</sub> ENMs is clearly needed, as these and other unregulated nanomaterials come into wider use.

## ENM research programs funded by NIEHS

After outlining problems unique to ENM research, such as developing reliable assays to test ENM toxicity and addressing the numerous types of ENMs in use, Nadadur described the NIEHS ENM research program. NIEHS has established a range of goals and funding opportunities for laboratories to investigate ENMs.



*Host Fenella Saunders, above, is senior editor of American Scientist. With support from the North Carolina Biotechnology Center, the journal hosts presentations each month from RTP area scientists working in a range of fields. (Photo courtesy of Steve McCaw)*



*Held in an intimate venue at Sigma Xi, the monthly lecture series attracts science communicators from nearby federal agencies, such as NIEHS, area universities and museums, and non-profit organizations concerned with health and scientific research. (Photo courtesy of Steve McCaw)*

One arm of the Nano Grand Opportunity grant program focused on assay development and exposure models ([see story](#)), while the NIEHS Centers for Nanotechnology Health Implications Research Consortium has aimed to bring together ENM researchers funded through various grants programs, including research project grants and Challenge Grants ([see story](#)).

The talk concluded with a number of questions from the audience. One audience member expressed surprise at the prolific use of ENMs, considering their unknown effects on human health. Nadadur's talk clearly made an impression on the writers and communicators in attendance that potential adverse health risk posed by ENM exposure, though not currently as hot a topic in the media as the new technology's potential, merits a much closer look.

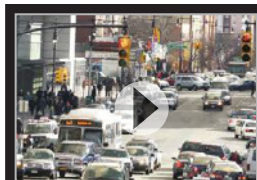
(Heather King, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Laboratory of Structural Biology Protein Expression Core.)

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## New studies offer insight into effects of air pollution on children

By Eddy Ball

Two new NIEHS-funded studies, led by researchers at Columbia University (CU), link urban air pollution with asthma risk and behavioral problems in children. In their conclusions, both research teams called for action and further study of these important environmental public health problems, as a step toward primary prevention.



### Linked video:

[Watch a Wall Street Journal report on the health effects of air pollution and ongoing research and prevention efforts by scientists at Columbia University \(04:03\)](#)

(Launches in new window)

Download Media Player: Flash [?](#)

The studies were led by faculty in CU's NIEHS-funded [Columbia Center for Children's Environmental Health \(CCCEH\)](#) — assistant professor of Environmental Health Sciences [Matthew Perzanowski, Ph.D.](#), an asthma specialist, and CCCEH Director [Frederica Perera, Dr.P.H.](#)

### Air pollution and health in two New York cohorts

The first [study](#), led by Perzanowski and published online in the *Journal of Exposure Science and Environmental Epidemiology*, studied air pollution from truck traffic and low-quality residual oil use, specifically airborne black carbon (BC) in indoor air and the respiratory health of children in the NYC [New York City] Neighborhood Asthma and Allergy Study. The researchers found an association between BC and high asthma prevalence neighborhoods, where as many as 18 percent of young children have the condition.



*Perera plans to follow the children in her study through age 12, so that subsequent testing will provide additional insights into the longer term development outcomes of children in the cohort. (Photo courtesy of Columbia University)*

The second [study](#), led by Perera, reported a significant association between prenatal exposure to polycyclic aromatic hydrocarbons (PAHs) and attention deficit and symptoms of anxiety and depression among children ages 6-7 in the CCCEH longitudinal cohort study. The findings appeared online in the journal *Environmental Health Perspectives*.

### **Black carbon — incomplete combustion of diesel and heating oil**

Perzanowski's team measured fractional exhaled nitric oxide (FeNO), a marker of subclinical changes in airway inflammation characteristic of asthma, in its cohort of 240 children ages 7-8. The researchers also collected and analyzed samples of bed dust and black carbon during home visits.

The researchers also used GIS data to characterize truck traffic and heating oil patterns for high asthma prevalence neighborhoods (11-18 percent) and low asthma prevalence neighborhoods (3-9 percent). They found a strong association between airborne BC in homes and both neighborhood asthma prevalence and FeNO, adding support to calls for regulations in New York to further reduce the burning of low-grade oil for domestic heating.

### **Exposure to PAH from fossil fuel, tobacco, and other organic material**

In addition to assessments of child behavior using the Child Behavior Checklist, a widely-used method of identifying problem behavior in children, Perera's group estimated prenatal PAH exposure by personal air monitoring during pregnancy and measured DNA adducts in maternal cord blood specific to benzo[a]pyrene, a representative PAH that can cross the placental barrier. The team used an investigator-administered questionnaire to collect demographics, health, environment, and dietary PAH at several time points, beginning with the last trimester of pregnancy.

In this first report of associations between child attention and behavioral problems, and two complementary specific measures of prenatal PAH exposure, the researchers followed 253 children *in utero* to ages 6-7, expanding earlier findings of developmental delays and risk for reduced IQ among children exposed to PAHs.

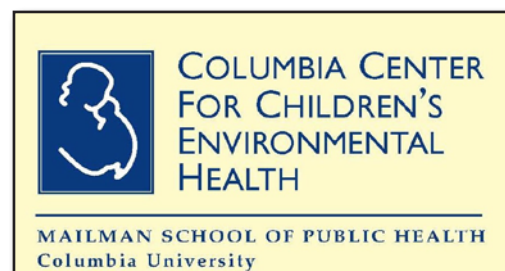
### **Focus on prevention through regulation and healthier homes**

In comments about their studies, the researchers offered guidance to parents and physicians about ways to prevent the adverse effects of exposure to indoor and outdoor air pollution, while strengthening the case for new government regulations to help protect the respiratory and neurobehavioral health of children in New York.

"This study adds to the evidence that further public health interventions on oil and truck emissions standards and the use of dirty oil may be warranted," Perzanowski argued in a CU [press release](#). "I think clinicians should be aware of the information about these environmental pollutants and should provide helpful tips to their patients," Perera also observed in another CU [press release](#).



*Perzanowski noted that the unequal distribution of incomplete combustion byproduct sources within a single city leads to differences of exposure even among communities with similar socioeconomic status. Perera and several members of the CCCEH were co-authors on the study (Photo courtesy of Columbia University)*



*Along with better education by clinicians, parents can take measures at home to improve air quality, such as eliminating mold, secondhand smoke, and other components of indoor air pollution. CCCEH provides free information [online](#) about ways to make homes healthier.*

In addition to supplemental grant and foundation support, the studies were funded by a number of NIEHS grants, including ones led by Perzanowski, “[Risk Factors Accounting for Neighborhood Differences in Asthma Prevalence](#),” and Perera, “[Developmental Effects of Early-life Exposure to Airborne PAHs](#).”

#### *Citations:*

Cornell AG, Chillrud SN, Mellins RB, Acosta LM, Miller RL, Quinn JW, Yan B, Divjan A, Olmedo OE, Lopez-Pintado S, Kinney PL, Perera FP, Jacobson JS, Goldstein IF, Rundle AG, Perzanowski MS. 2012. Domestic airborne black carbon and exhaled nitric oxide in children in NYC. *J Expo Sci Environ Epidemiol*; doi: 10.1038/jes.2012.3 [Online 29 February 2012].

Perera FP, Tang D, Wang S, Vishnevetsky J, Zhang B, Diaz D, Camann D, Rauh V. 2012. Prenatal Polycyclic Aromatic Hydrocarbon (PAH) Exposure and Child Behavior at age 6-7. *Environ Health Perspect*; doi: 10.1289/ehp.1104315 [Online 22 March 2012].

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## Temperature variability tied to shorter life expectancy

*By Nancy Lamontagne*

Researchers led by NIEHS grantee [Joel Schwartz, Ph.D.](#), report that increasing variability in summer temperatures may reduce the life expectancy of elderly people with chronic medical conditions. Greater temperature variability is expected to occur because of climate change, and the researchers estimate that just a 1 degree Celsius increase in temperature variability could result in approximately 14,000 additional deaths per year in the groups included in the study.

Previous studies examined heat waves, or the effects of hot weather on day-to-day mortality, but these studies do not show whether the shortening of life expectancy from the heat-related event is significant. “If the lives lost on hot days were only shortened by, for example, a few weeks, then there would be no noticeable impact on the annual average mortality rate,” said Schwartz, a professor of environmental epidemiology at the Harvard School of Public Health. “Our study is the first cohort analysis of the effects of long-term differences in temperature and mortality rates.”

The [study](#) is the first publication to come from the NIEHS-funded Climate Change and Human Health research program ([see story](#)), which was launched in 2010. This program funds research examining the environmental risk factors linked to climate change that impact the health of people, including extreme heat and other changing weather patterns, and increased exposures, such as air pollution and harmful chemicals.

“A main goal of the NIEHS Climate Change and Human Health Program is to identify specific factors that may increase population vulnerability to health impacts of climate change,” said NIEHS Health Scientist Administrator Caroline Dilworth, Ph.D. “To this end, study findings like these help broaden our understanding of the populations at greatest risk.”



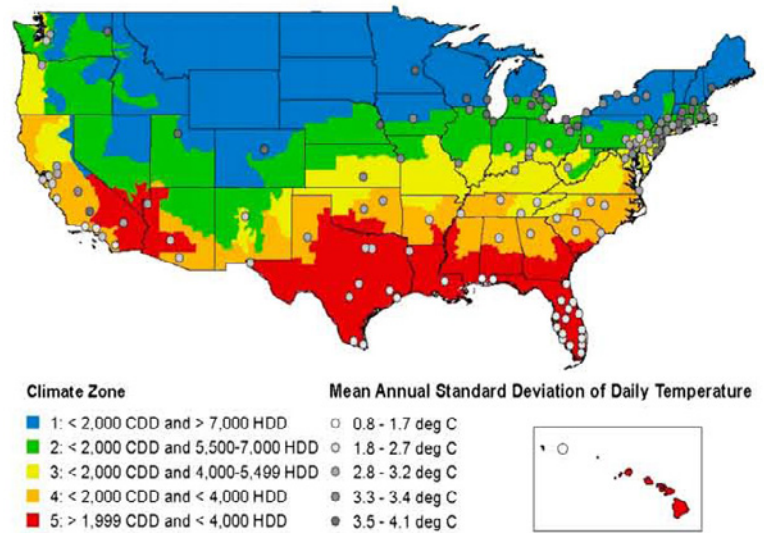
*Schwartz's study confirms that increased weather variability is a serious public health concern. (Photo courtesy of Steve McCaw)*

## Looking long term

The Harvard researchers used Medicare data from 1985 to 2006 to follow the health of 3.7 million chronically ill people over age 65. They looked at whether year-to-year differences in the annual average mortality rates related to year-to-year differences in the variability of summer temperatures.

The researchers analyzed each of the 125 cities included in the study separately.

“This is important because people likely acclimate to usual patterns in their city,” said Schwartz. “It also avoids confounding factors that differ across cities.” The researchers also took into account other factors such as winter temperature variance, heat waves, ozone levels, and individual risk factors.



*The study included people living in cities, show as dots, in a variety of climate zones. (Photo courtesy of Joel Schwartz)*

The results showed that each 1 degree Celsius increase in summer temperature variability increased the death rate for elderly people with chronic conditions between 2.8 and 4.0 percent, depending on the condition. The mortality risk was 1 to 2 percent greater for those living in poverty and for African-Americans.

Contrary to prior studies of heat waves and hot days, the summer temperature variability in this study seemed to have a greater effect in southern cities. Residents in warmer cities might be more acclimated to hot weather but less able to handle variable weather. “That is important for public health, because the heat wave studies suggested that these cities had less to worry about, and there may have, therefore, been less attention to the issue in these cities,” said Schwartz.

## Prevention

Incorporating more green space could help offset the effects of temperature variability. The study showed that mortality risk was 1 to 2 percent lower for people living in cities with more green space. Schwartz explained that the sensitivity to variable summer temperatures likely occurs because people cannot get into a routine in regard to activities, appropriate clothing, and air conditioning usage. Local weather broadcasts could help people adjust, by emphasizing when temperatures will be noticeably different and suggesting that people adapt their clothing and activity patterns accordingly. However, this type of intervention needs testing.

The researchers plan a number of directions for future research. “We need to look at elderly people without pre-existing medical conditions and with different conditions, such as neurological diseases,” he said. “Why African-Americans are more vulnerable is a key question.” Further study is also needed to understand the physiology of responses to temperature variability and why certain effects occur.

*Citation:* [Zanobetti A, O’Neill MS, Gronlund CJ, Schwartz JD. 2012. Summer temperature variability and long-term survival among elderly people with chronic disease. Proc Natl Acad Sci U S A; doi:10.1073/pnas.1113070109 \[Online 9 April 2012\].](#) [Summary](#)

(Nancy Lamontagne is a science writer with MDB, Inc., a contractor for the NIEHS Division of Extramural Research and Training, Superfund Research Program, and Worker Education and Training Program.)

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# Early-life exposure to secondhand smoke affects girls more than boys

By Amanda Harper

The negative health effects of early-life exposure to secondhand smoke appear to impact girls more than boys — particularly those with early-life allergic sensitization, according to new NIEHS-funded [research](#) from the University of Cincinnati (UC) College of Medicine.

Epidemiologists with UC's [Cincinnati Childhood Allergy and Air Pollution Study \(CCAAPS\)](#), funded by NIEHS, found that children exposed to high levels of secondhand smoke who also had allergic sensitizations during early childhood are at greater risk for decreased lung function at age 7 compared to children who had not developed allergic sensitizations by this age.

Additionally, lung function among girls was six times worse than in boys who were exposed to similar levels of both secondhand smoke and allergen sensitization.

## Timing is crucial

“Our study shows that the timing of allergic sensitization is crucial because children who are sensitized by age 2 are more likely to suffer the greatest lung deficits during childhood as a result of secondhand smoke exposure,” explained Kelly Brunst, first author of the paper and a doctoral candidate in UC’s division of epidemiology and biostatistics. “This association was not observed at age 4 or 7, emphasizing the importance of this critical window for lung development.”

The team’s findings were published online March 21 in the journal *Pediatric Allergy and Immunology*.

This is the first study to explore the differential gender effects of secondhand smoke exposure using an internal biomarker for secondhand smoke — hair cotinine, a product of nicotine metabolism — while also accounting for the importance of timing and extent of allergic sensitization on lung function.

Previous studies have estimated that one in four children in the United States living in a home with at least one smoker have cotinine concentrations more than twice as high as those living with nonsmoking adults. Secondhand smoke exposure during childhood has also been associated with respiratory illness, decreased lung function, and asthma development or exacerbation.



*Kelly Brunst was first author on the study, which underscores the importance of exposures during critical windows of development and adds support to the two-hit hypothesis about host susceptibility. (Photo courtesy of UC)*



*Veteran grantee LeMasters is also a member of the National Advisory Environmental Health Sciences Council, which meets three times each year at NIEHS. (Photo courtesy of UC)*

## A role for gender

“Our results provide valuable information regarding the interwoven relationships between early-life exposure to secondhand tobacco smoke, allergic sensitization, gender, and lung function,” said [Grace LeMasters, Ph.D.](#), UC professor of environmental health and principal investigator of CCAAPS.

“It’s likely that the complex interaction between secondhand smoke and pulmonary function loss in boys and girls is ultimately dependent on the timing of exposure as well as the child’s total load in relationship to cumulative risk factors — exposures, allergic sensitization, asthma status, genetic susceptibility, and sex hormones.”

CCAAPS is a long-term childhood study examining the effects of environmental exposures on respiratory health and allergy development. All infants in the study had at least one parent with known allergies and were followed from infancy until age 7.

For this study, researchers examined a population of 476 children in the Greater Cincinnati metropolitan area identified from birth to be at increased risk for allergies based on family history and proximity to major roads. Hair samples were collected at age 2 and 4 to measure average cotinine concentrations. At age 7, all children had lung function and asthma diagnosis testing. This information was then correlated with data about allergy sensitization collected through annual skin prick allergy testing, self-report questionnaires about allergy symptoms, and the home and school environment.

Collaborators in the study include UC’s Linda Levin, David Bernstein, M.D., James Lockey, M.D., Manuel Villareal, M.D., Jeff Burkle, and Roy McKay, as well as Gurjit Khurana Hershey, M.D., Patrick Ryan, M.D., and Jocelyn Biagini Meyers, Ph.D., of Cincinnati Children’s Hospital Medical Center. Sherry Evans of the Bernstein Clinical Research Center also contributed to this study.

*Citation:* [Brunst KJ, Ryan PH, Lockey JE, Bernstein DI, McKay RT, Khurana Hershey GK, Villareal M, Biagini Myers JM, Levin L, Burkle J, Evans S, LeMasters GK.](#) 2012. Unraveling the relationship between aeroallergen sensitization, gender, second-hand smoke exposure, and impaired lung function. *Pediatr Allergy Immunol*; doi: 10.1111/j.1399-3038.2012.01292.x [Online 21 March 2012].

(Amanda Harper is a public information officer in the Office of Public Relations and Communications at the UC Academic Health Center. For more information about this study, contact Harper by phone at 513-558-4657 or by email at [amanda.harper@uc.edu](mailto:amanda.harper@uc.edu).)

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## Arsenic turns stem cells cancerous, spurring tumor growth

*By Robin Mackar*

NIEHS researchers have discovered how exposure to arsenic can turn normal stem cells into cancer stem cells and spur tumor growth. The [findings](#) were published April 4 online in the journal *Environmental Health Perspectives*.

Inorganic arsenic, which affects the drinking water of millions of people worldwide, has been previously shown to be a human carcinogen. A growing body of evidence suggests that cancer is a stem cell-based disease. Normal stem cells are essential to normal tissue regeneration and to the stability of organisms and processes. But cancer stem cells are thought to be the driving force for the formation, growth, and spread of tumors.

Michael Waalkes, Ph.D., and his team at the National Toxicology Program Laboratory had previously shown that normal cells become cancerous when they are treated with inorganic arsenic. This new study shows that when these cancer cells are placed near, but not in contact with normal stem cells, the normal stem cells very rapidly acquire the characteristics of cancer stem cells. It demonstrates that malignant cells are able to send molecular signals through a semipermeable membrane, where cells can't normally pass, and turn the normal stem cells into cancer stem cells.

### **The key to cancer proliferation**

“This paper shows a different and unique way that cancers can expand by recruiting nearby normal stem cells and creating an overabundance of cancer stem cells,” said Waalkes. “The recruitment of normal stem cells into cancer stem cells could have broad implications for the carcinogenic process in general, including tumor growth and metastases.”



*Lead researcher Michael Waalkes (Photo courtesy of Steve McCaw)*

This reveals a potentially important aspect of arsenic carcinogenesis and may help explain observances by researchers working with arsenic that arsenic often causes multiple tumors, of many types, to form on the skin or inside the body.

Waalkes' lab started working with stem cells about five years ago. The researchers used a prostate stem cell line, not embryonic stem cells.

“Using stem cells to answer questions about disease is an important new growing area of research. Stem cells help to explain a lot about carcinogenesis, and it is highly likely that stem cells are contributing factors to other chronic diseases,” Waalkes said.

Stem cells are unique in the body. They stay around for a long time and are capable of dividing and renewing themselves. “Most cancers take 30 or 40 years to develop,” said Linda Birnbaum, Ph.D., director of NIEHS and NTP. “It makes sense that stem cells may play a role in the developmental basis of adult disease. We know that exposures to toxicants during development and growth can lead to diseases later in life.”

Next, the laboratory team will look to see if this finding is unique to arsenic or if it is applicable to other organic and inorganic carcinogens.

*Citation:* [Xu Y](#), [Tokar EJ](#), [Sun Y](#), [Waalkes MP](#). 2012. Arsenic-transformed malignant prostate epithelia can convert noncontiguous normal stem cells into an oncogenic phenotype. *Environ Health Perspect*; doi:10.1289/ehp.1204987 [Online 4 April 2012].

(Robin Mackar is the news director in the NIEHS Office of Communications and Public Liaison.)

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# Does diet alter damage from environmental exposures?

By Angela Spivey

Can something as simple as what people eat determine whether powerful chemicals, such as polychlorinated biphenyls (PCBs), damage their bodies? Possibly so, according to a new NIEHS-funded study by [Bernhard Hennig, Ph.D.](#), professor of nutrition and toxicology and director of the Superfund Research Program (SRP) at the University of Kentucky (UK), and other researchers.

“The evidence is very strong from animal studies and correlation studies that those who are more nutritionally sound are more resistant to chemical insults,” Hennig said. Specific elements in the diet can either stop or promote some of the damaging processes, such as oxidative stress and inflammation, which follow exposure to many environmental chemicals.

## Prevention through nutrition

Animal studies have shown that PCB exposure can induce atherosclerosis, for example. But when Hennig fed mice an olive oil-enriched diet and then exposed them to PCBs, the chemical had little effect on their fatty acid profiles. Mice that ate a corn oil-enriched diet showed significant changes in serum fatty acids after PCB exposure. So the type of fat in the diet, not just the amount of fat, may make a difference in the cell damage that is triggered by environmental chemicals. In addition, Hennig and other researchers have found that antioxidants, such as vitamin E and flavonoids, as well as a high ratio of omega-3 to omega-6 fatty acids, can reduce cell damage caused by PCBs and other pollutants.

This and other evidence leads some researchers to recommend that future environmental health research and pollutant risk assessment approaches incorporate nutrition and dietary practices. “In the past, risk assessment was based on one chemical, but we now know that it’s much more complicated than that — we are exposed to mixtures of chemicals,” Hennig said. Incorporating nutrition into risk assessment of environmental chemicals extends that idea. “Other factors, such as nutrition, may either increase the response to chemicals or reduce it,” Hennig said.

The idea that diet contributes to health is ancient, but efforts to understand how specific nutrients influence disease risk from environmental pollutants is novel, stated William Suk, Ph.D., director of the NIEHS Superfund Research Program. “If we are going to assess the risk of an individual, we have to be able to



*Hennig, right, gave a talk about nutrition and host susceptibility at NIEHS in 2011 ([see story](#)), hosted by Suk.*



*UK SRP program staff spread the word about prevention during outreach events, such as this one near Dayhoit, Ky., the location of one of the state’s Superfund sites. (Photo courtesy of Lisa Gaetke)*

consider a variety of factors and cofactors, and one of the big things is what we eat and drink,” Suk said. “Understanding nutrition, and how it modulates risk and potentially prevents disease, is part of the new NIEHS strategic plan currently under review.”

### **Expanding research with human subjects**

Much of the evidence for the nutrient-pollutant connection comes from animal studies. But well-defined, prospective epidemiological studies with repeated measures of exposures to both environmental chemicals and nutrients are needed, according to Somdat Mahabir, Ph.D., program director with the Epidemiology and Genetics Research Program of the National Cancer Institute. Mahabir is interested in epidemiological research aimed at understanding whether dietary patterns and specific nutritional factors are useful in offsetting a portion of the disease risk attributable to environmental pollutants.

“The idea that nutritional factors can modulate the toxicity of environmental pollutants and, thus, have consequence for human disease risk is an interesting concept with potentially important public health significance. However, well-defined epidemiological studies to test this hypothesis have not been done, due to methodological challenges,” Mahabir said (see text box). Data from human prospective studies could be used to model, for example, whether people exposed to high levels of pollutants and high levels of dietary fat are at higher risk for diseases, such as cancer, than individuals exposed to high levels of pollutants and low levels of fat.

Even with the best remediation efforts, it’s nearly impossible to remove all the chemicals at a given site, according to Hennig. Nutrition may become the simplest form of risk reduction. The UK SRP uses nutrition education as part of its community engagement efforts. “Nutrition may be a very meaningful way to make people and animals less vulnerable to chemical stressors,” Hennig said.

### *Citations:*

Hennig B, Ormsbee L, McClain CJ, Watkins BA, Blumberg B, Bachas LG, Sanderson W, Thompson C, Suk WA. 2012. Nutrition can modulate the toxicity of environmental pollutants: implications in risk assessment and human health. *Environ Health Perspect*; doi: 10.1289/ehp.1104712 [Online 22 February 2012].

Hennig B, Reiterer G, Majkova Z, Oesterling E, Meerarani P, Toborek M. 2005. Modification of environmental toxicity by nutrients: implications in atherosclerosis. *Cardiovasc Toxicol* 5(2):153-160.

(Angela Spivey is a contract science writer for the NIEHS Superfund Research Program.)

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## **Teasing out the role of nutrition in risk assessment**

There are many other challenges involved in incorporating nutrition into risk assessment. In cross-sectional human studies that have been conducted, the effects of nutritional interventions, such as antioxidants, have been less robust than in animal studies, and more research is needed to understand this variability in humans. This variability is likely influenced by many factors, including genetic polymorphisms and epigenetic effects of nutrition and pollutants, Hennig and colleagues noted, adding that risk assessment and nutritional intervention should consider the implications of research in nutrigenetics and nutrigenomics. Also of concern is the long-term effect of supplementing nutrients that can be used as therapeutics, such as antioxidants and fatty acid supplements. In addition, there is a need to learn more about the bioactive targets that various nutrients act upon.

# GEMS goes transdisciplinary with spring meeting

By Eddy Ball

The [Genetics and Environmental Mutagenesis Society \(GEMS\)](#) continued its tradition of promoting leading-edge science, at its spring meeting April 24 at the U.S. Environmental Protection Agency (EPA) in Research Triangle Park, N.C. However, unlike previous meetings in the spring and fall each year, this latest meeting's agenda cast a much wider net, featuring speakers with interests ranging from toxicology and environmental engineering to comprehensive biofuels development and data management.

The meeting opened with a welcome by GEMS President Nagu Keshava, Ph.D., who introduced the program's organizer, GEMS President-Elect [Lyle Burgoon, Ph.D.](#)

## An abundant new energy source that could endanger public health

The first speaker of the program not only addressed a headline-grabbing topic in environmental health, hydraulic fracturing, or fracking, he has also been a part of the headlines. Duke University professor [Robert Jackson, Ph.D.](#), has taken a responsible course with his research on shale gas, hydraulic fracturing, and environmental health, angering people on both sides of the controversy with his refusal to abandon his scientific objectivity.

Early in his talk, Jackson focused on the central issue involved in fracking. "The gas doesn't just come out," Jackson said. "You have to coax it out."

People are justifiably concerned, Jackson explained, about effects of leaking methane gas and the millions of gallons of chemically laden water used in fracking on groundwater, air quality, and earthquake tremors. But as with any form of energy, people need to balance risks and benefits.

## Nano — where biology and toxicology meet physics

Veteran NIEHS grantee Martin Philbert, Ph.D., assumed his self-described role as a fly in the ointment, with a dazzling presentation on the potential benefits and health implications of engineered nanomaterials (ENMs).



*After organizing two meetings of her own in 2011, as then president-elect, Keshava was in high spirits as she introduced her successor, welcomed members to the meeting, and looked forward to watching as Burgoon moderated the program. (Photo courtesy of Steve McCaw)*



*According to Burgoon, the agenda was designed to highlight emerging environmental issues — ones that are changing people's everyday lives and challenging preconceived notions about such topics as dose and exposure. Like Keshava, Burgoon is a researcher at EPA. (Photo courtesy of Steve McCaw)*

According to Philbert, there are no truly informative studies, yet, of the toxicology of ENMs, and no comprehensive concept of how physical characteristics impact dose in regard to ENMs. “We are spraying wildly in the dark,” he told the audience.

Philbert conducts his research at the University of Michigan, where some of his colleagues are also exploring new applications for ENMs in medicine. He balanced his precautionary look at nanotoxicology with a demonstration of the benefits people can expect from therapeutic applications of the new materials, such as restoring sight to blind retinæ by activating calcium and potassium channels, countering buildup of proteins involved in neurodegenerative disease, and treating chemical and radiation therapy-resistant cancers.

### Creating a grassroots biofuels industry in North Carolina

Steven Burke, president and chief executive officer of the [Biofuels Center of North Carolina](#), devoted his presentation to a description of what many would consider an impossible task — establishing a new sustainable energy production network and market, for locally produced biofuels, from organic matter other than corn, where none existed in 2007 — all in the space of ten years.

“The challenge [of this kind of revolutionary program] has, to date, not be solved in America,” he conceded. “And we don’t have a model for this,” he said of a program that promises to profoundly affect the political, cultural, environmental, climatic, and agricultural landscape of North Carolina.

### Risk and benefit in water purification

North Carolina State University professor [Detlef Knappe, Ph.D.](#), concluded the scientific portion of the meeting with a talk on human health risks resulting from advances in one of the greatest public health achievements in modern history — the filtration and disinfection of municipal drinking water. He began with a description of the introduction of filtration and chlorination, which helped reduce mortality from waterborne diseases by between one-half, for the entire population, to three-quarters, for infants, before moving into the unanticipated side effects from disinfectant byproducts (DBPs) created during water treatment.

He said animal studies link some DBPs with liver and other cancers, and human epidemiological studies have found associations with bladder and colorectal cancers. “But there’s a bit of a disconnect here,” he said, and there’s a need for more research to establish health effects and to discover ways to improve treatment protocols to make water even safer.



*After discussing some of the strengths and weakness of alternative forms of generating power, Jackson left the audience with a central question to consider about preparing for future energy needs. “Where does the energy come from if you don’t do something like hydraulic fracturing?” he asked. (Photo courtesy of Steve McCaw)*



*At the beginning of his talk, Philbert promised to make at least one person in the audience angry by denying that there is currently any such thing as nanotoxicology. He argued that ENMs, because of their size, various shapes, manufacturing variability, and other physical properties, challenge the current single-dimensional paradigms of dose, mode of action, and gross physiological endpoints. (Photo courtesy of Steve McCaw)*

## Safeguarding scientific data

EPA information technology guru David Lyons is the first to admit that he's not a scientist, but what he does for the agency is an important part of enabling science to have its maximum impact now, and in the years to come, through development of EPA's new Laboratory Information Management System. As he explained during his talk at the GEMS meeting, his greatest challenges are not technological, but managerial. "It's really all about how to organize your stuff," Lyons said.

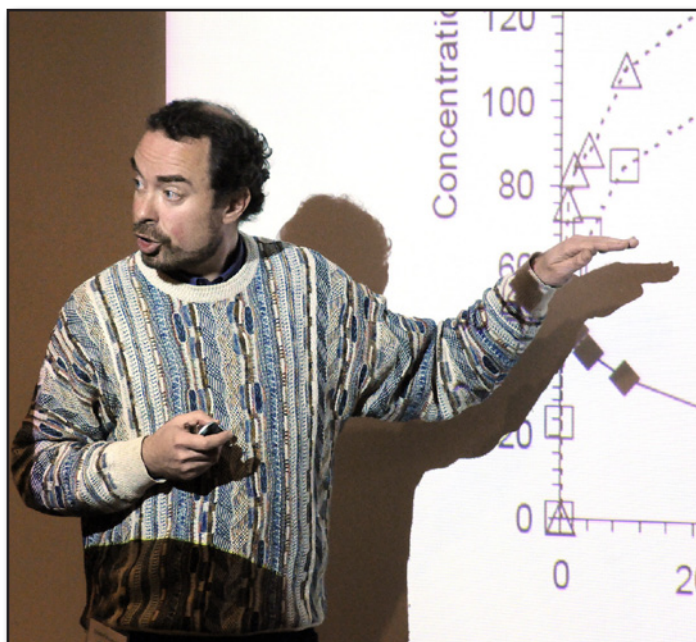
Lyons is leading EPA's scientific data management initiative that is creating a unified safe storage protocol for the hundreds of terabytes of information in existence in various storage formats on network drives, enterprise portals, servers, and Internet sites. He and his group are also working to develop the right set of metadata to effectively search the millions of files already in storage, and discover ways to avoid an increase in the 25 terabytes of data now archived and considered orphaned because the owner is unknown.

Lyon faces important challenges. Data generation has traditionally been a shortsighted and haphazard process, with individuals and groups producing information in various formats and storing it as inexpensively and conveniently as possible. When someone copies data from a personal computer to a storage device, Lyons said, the creation date changes, forcing the archiver to search for the earliest date of modification. Under current procedures, when employees resign or retire, their accounts are deleted along with the owner identification, orphaning the data.

But things are beginning to change. The federal government has intensified the push for data management and data integration, and the National Science Foundation now requires a data management plan with all new grant proposals, which could set a precedent that will encourage more cooperation, on the agency level, with plans to preserve data in an accessible form for researchers in the future.



*In his effort to describe the challenge of developing sufficient amounts of non-corn biofuels, to make up 25 percent of liquid energy needs by 2012, Burke neglected to mention possible adverse effects or benefits for public health, but those topics have not escaped some EPA researchers. (Photo courtesy of Steve McCaw)*



*Knappe pointed out several ways to improve water treatment, such as adding superfine powdered activated carbon filters to remove natural organic matter prior to disinfection, new disinfecting protocols, and infrastructure improvements. Of the additional expense, he said, "If we want higher quality water, we have to think about paying for it." (Photo courtesy of Steve McCaw)*



*To underscore the need for effective data management, Lyons shared examples of just how sloppy scientists have been about data storage. He told the story of one unfortunate researcher who inadvertently erased an entire project's data by setting his device down next to the magnet in a loud speaker. (Photo courtesy of Steve McCaw)*



*NIEHS biologist Cindy Innes, a GEMS veteran and former officer, was on hand for the interesting mix of talks. (Photo courtesy of Steve McCaw)*



*So was NIEHS Senior Advisor Allen Dearry, Ph.D., who hasn't attended many previous meetings, but was intrigued by this one's unusual agenda. (Photo courtesy of Steve McCaw)*



*EPA researcher Brian Chorley, Ph.D., center, was one of the many EPA employees attending the meeting. Chorley completed his postdoc at NIEHS, before joining EPA, and he is currently a GEMS officer. (Photo courtesy of Steve McCaw)*

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# Harris discusses novel target to promote HIV eradication

By Jeffrey Stumpf

HIV therapeutics are currently capable of suppressing virus replication to virtually undetectable levels and enabling patients to lead near-normal lives. However, in a talk April 16 at NIEHS, cancer geneticist [Reuben Harris, Ph.D.](#), reminded attendees of the obvious reason to continue studying cellular processes that could be targets for novel therapeutic strategies.

“We haven’t cured HIV, yet,” Harris stated. “It is still a big problem around the globe for human health and economically.” Harris spoke as part of the Laboratory of Molecular Carcinogenesis (LMG) Fellows Invited Guest Lecture Series. NIEHS fellow Kathleen Richter, Ph.D., and her colleagues in the Somatic Hypermutation Group hosted Harris.

As an associate professor at the University of Minnesota, Harris has maintained a long-standing interest in DNA replication and mechanisms that increase mutation. Studying immune defenses to the virus that causes AIDS satisfies his intellectual curiosity with the possibility of improving human health.

“The long term goal is a cure. The short term goal is to learn a lot about the molecular mechanisms and the details about how these proteins inhibit virus replication, and how the virus fights back,” Harris explained.

## The battle for HIV replication: Human APOBEC versus HIV Vif

Harris focused his talk on the role of the family of APOBEC proteins in rendering the HIV virus non-infectious. APOBEC deaminates deoxycytosines in single-stranded DNA, thus converting them into deoxyuracils and leading to mutations that can inactivate the virus. HIV counters the attack by the APOBECs using the Vif protein, which signals the ubiquitin ligase cascade to target the degradation of APOBEC proteins.

There are many APOBEC proteins that can potentially inhibit viral replication. APOBEC3G is known to inhibit HIV infectivity in cultured cells. Using new viral vector techniques to ablate genes in human cell lines, Harris showed that APOBEC3D, 3F, and 3H, in addition to APOBEC3G, also contribute to the human defense against HIV infection.

Reconstituting the degradation of the APOBEC proteins by Vif remained elusive until recently, according to Harris. The *in vitro* studies were lacking a cofactor, which Harris demonstrated was the human protein CBFbeta. HIV is thought to recruit the CBFbeta protein to aid the stability, or proper folding, of the HIV Vif protein.



*Harris described one of many studies on the role of APOBEC in fighting off HIV infections. (Photo courtesy of Steve McCaw)*



*LMG fellow Shay Covo, Ph.D., instigates a fascinating discussion about the possibility of population genetic studies of APOBEC variants that may confer resistance to HIV infections. (Photo courtesy of Steve McCaw)*

## To mutate or not to mutate

Immune responses and therapies against HIV are stymied by the unrelenting mutation rate that renders the viral genome a moving target. The relationship between the mutation-promoting APOBECs and Vif exemplifies the delicate balance of how mutations can destroy the virus or make it more difficult to control. Harris mentioned the idea of targeting APOBEC proteins for a novel HIV therapy, but asked whether it was better to intensify the mutagenic process or deter it.

On one hand, inhibiting proteins in the APOBEC degradation pathway, as Harris points out, may unleash a mutation load that the virus could not overcome. “I would call it therapy by hypermutation,” proposed Harris. “If you can stop degradation of APOBEC proteins, you would have a very high level of virus mutations.”

On the other hand, Harris postulated that eliminating APOBEC completely may stagnate the viral genome, making it more vulnerable to natural and therapy-based defenses. “One could imagine inhibiting APOBECs as a novel strategy,” Harris surmised. “If you decrease viral mutation rates by taking away all of APOBECs contribution, you may have a smaller swarm of viruses that the immune response could effectively clear.”

Following the latter choice, Harris announced the first class of APOBEC3G inhibitors from small molecule screens. “The molecules bind to the pocket adjacent to the active site and covalently react with the cytosine to prevent deamination,” Harris reported. “The inhibitor is like a shield around the cytosine.” Future studies will determine whether therapy by hypomutation will become a reality in the fight against HIV infection.

(Jeffrey Stumpf, Ph.D., is a research fellow in the NIEHS Laboratory of Molecular Genetics Mitochondrial DNA Replication Group.)

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*Shown, right to left, LMG postdoctoral fellow, Kin Chan, Ph.D. (right), joins members of the Somatic Hypermutation group, Chuancang Jiang, Ph.D., Ming-Lang Zhao, Ph.D., and Madhumita Ray for Harris's presentation. (Photo courtesy of Steve McCaw)*

## BPA exposure traced to abnormal heart rhythms

*By Thaddeus Schug*

A new [study](#) by NIEHS grantees reports that the chemical bisphenol A (BPA), commonly found in many plastic household items, has been linked to increased frequency of arrhythmias, or heartbeat irregularities, in animals.

Plastics made with BPA are used in many consumer products, including food and beverage containers, toys, eyeglasses, computers, kitchen appliances, and medical equipment. Epoxy resins containing the chemical are used in dental work and in metal coatings for food cans, pipes, cars, dairy equipment, office equipment, and other metal products. BPA is also used in the production of certain flame retardants and as a color developer in some thermal receipt paper.

While the findings of this study are intriguing, this is only one of many NIEHS-funded studies currently underway to better understand if there are health effects related to BPA. A single study is not sufficient to make a determination about the health effects in humans.

### Experiments in rats and mice

Prior to their investigation, the effects of BPA on the heart were largely unknown, according to study co-authors Scott Belcher, Ph.D., and Hong-Sheng Wang, Ph.D., from the University of Cincinnati (UC) Department of Pharmacology and Cell Biophysics. The study reports that low doses of BPA and estrogen can act alone, or in combination, to increase arrhythmias in female rats and mice. Mice and rats in the study had normal heart rhythms at baseline, before administration of BPA or the estrogen, estradiol, Belcher said.

The investigators studied heart rhythms in both the working heart and in cultured heart muscle cells. In both models, exposure to BPA increased the frequency of arrhythmias in females but not males. Administration of estrogen alone also increased the frequency of arrhythmias in females.

Arrhythmias were most frequent in the female rats and mice, when they received both BPA and estrogen at levels normally found in female humans.

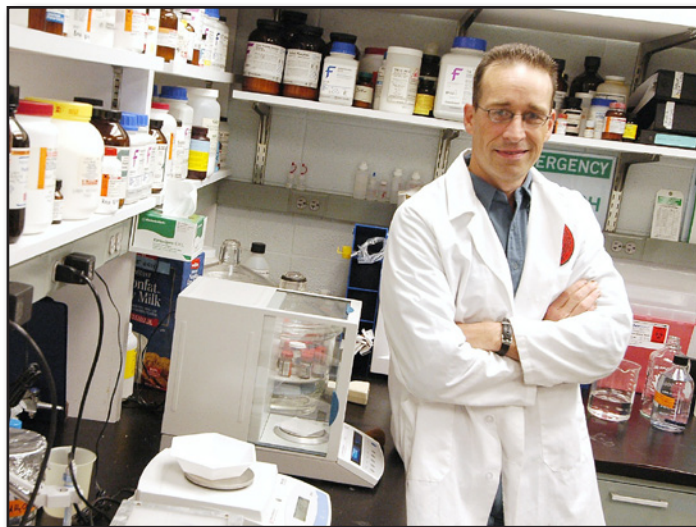
“We have identified a new possible risk for female heart health, caused by increased levels of estrogens in the body and exposure to the environmental estrogen BPA,” Belcher said.

### Heart rhythm irregularities

Arrhythmias occur when the heart beats too slowly or too fast, or when it skips heartbeats. These heart rhythm irregularities can cause fatigue, lightheadedness, fainting, or sudden cardiac death. If a fast heart rate affects the heart’s ability to pump, it can cause a heart attack.

“From a cardiac physiologist’s point of view, I think it is intriguing that a common environmental chemical can have such marked impact on the heart, as demonstrated in our study,” said Wang. Combined with recent epidemiological evidence, our work points to a potentially significant role of environmental BPA exposure in cardiovascular disease, particularly in females,” Wang added.

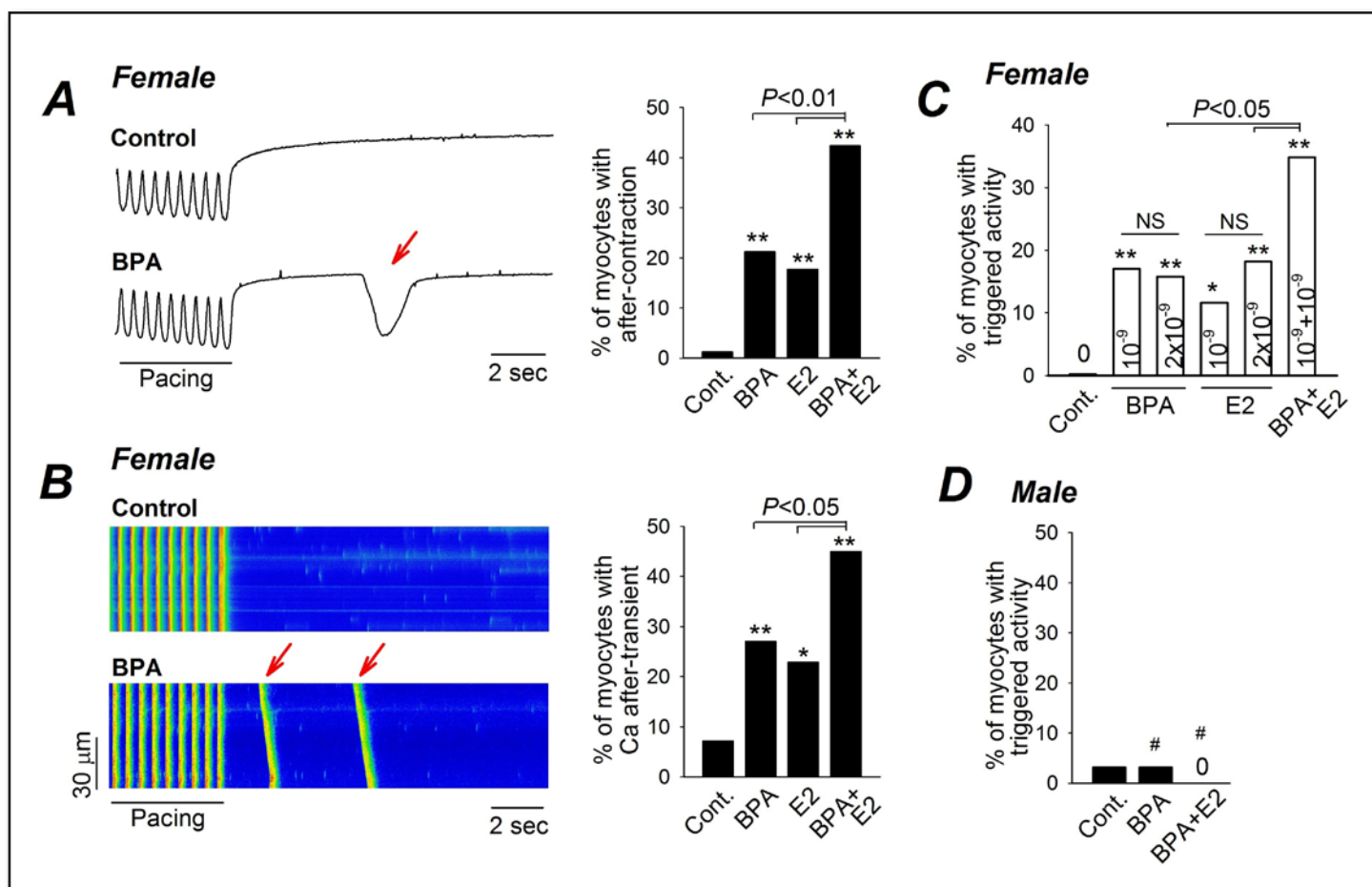
The rapid proarrhythmic effect of BPA was observed at very low doses, as low as subnanomolar or picomolar range, which is within the range of human BPA exposure, according to most epidemiological studies in the literature.



*Belcher is shown in his lab at UC. (Photo courtesy of UC)*



*Wang spoke at NIEHS in January at a meeting of grantees researching Bisphenol A ([see story](#)), where he presented his group’s findings. (Photo courtesy of Steve McCaw)*



These figures demonstrate how acute low dose exposures to BPA and estradiol promote arrhythmic events in female rat heart cells. (A) Low dose levels of BPA elicit spontaneous contraction in myocytes. (B) BPA exposure induces calcium transients. (C-D) Percentage of female and male myocytes with triggered activities following estradiol and BPA exposure. (Graphic courtesy of Hong-Seng Wang).

#### Citations:

Belcher SM, Chen Y, Yan S, Wang HS. 2012. Rapid estrogen receptor-mediated mechanisms determine the sexually dimorphic sensitivity of ventricular myocytes to 17 $\beta$ -estradiol and the environmental endocrine disruptor bisphenol A. *Endocrinology* 153(2):712-720.

Yan S, Chen Y, Dong M, Song W, Belcher SM, Wang HS. 2011. Bisphenol A and 17 $\beta$ -estradiol promote arrhythmia in the female heart via alteration of calcium handling. *PLoS One* 6(9):e25455.

(Thaddeus Schug, Ph.D., is a health scientist in the NIEHS Division of Extramural Research and Training (DERT) and a regular contributor to the Environmental Factor.)

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## Columbia University unveils NPL mapper

By Rebecca Wilson

Researchers at the NIEHS-funded Columbia University Superfund Research Program (SRP) have developed a new online [mapper](#) capable of displaying population and environmental characteristics of the areas surrounding

more than 1,500 hazardous waste sites on the U.S. Environmental Protection Agency's (EPA) National Priorities List (NPL). Meredith Golden led the research team in combining data from several agencies to create a clickable map with a powerful zooming function that allows users to learn about communities near NPL sites across the country.

Golden is a senior staff associate at the [Center for International Earth Science Information Network \(CIESIN\)](#), a center within The Earth Institute at Columbia University.

### Building a better application

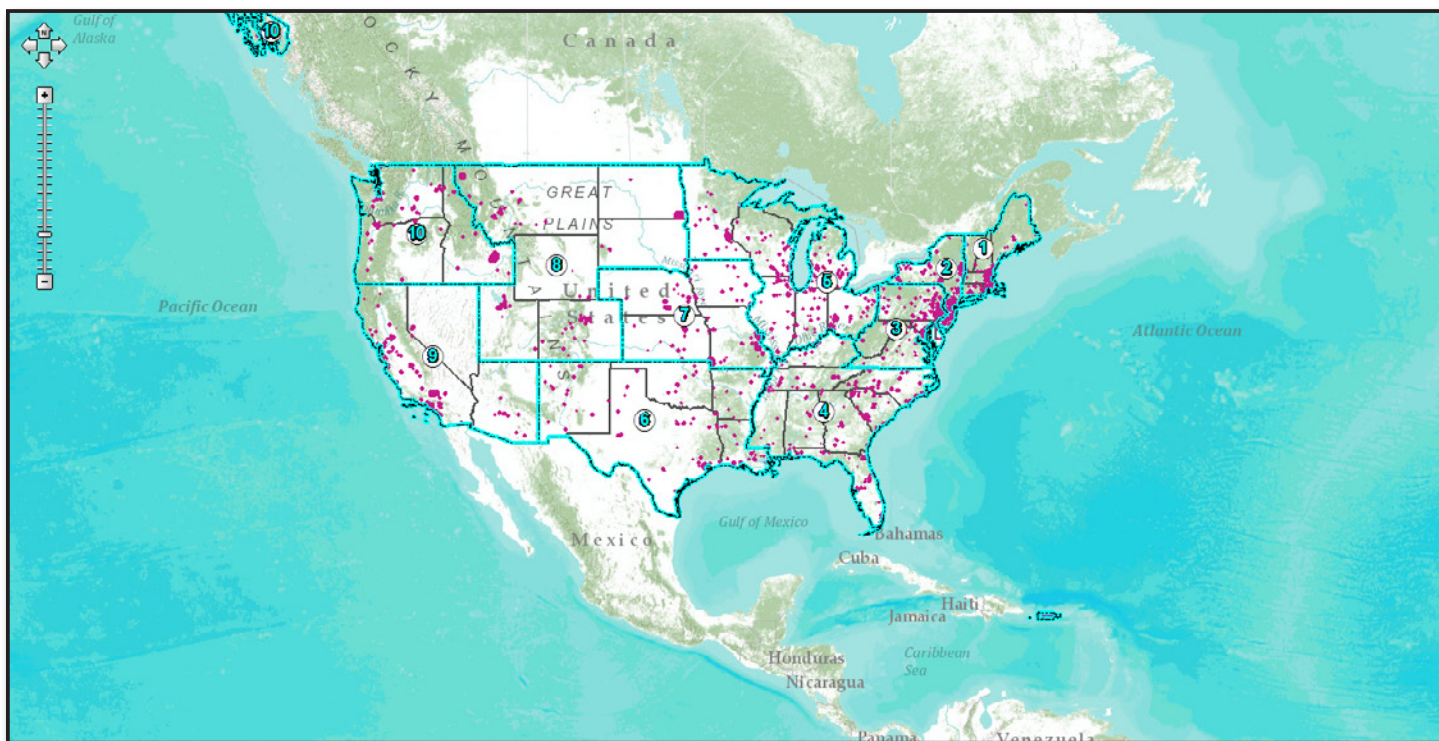
The researchers used Geographic Information System (GIS) mapping techniques to render data in a user-friendly way that is accessible to researchers, regulators, and the general public. Land use and environmental data are provided by the EPA, the Agency for Toxic Substances and Disease Registry, the U.S. Geological Survey (USGS), and other SRP centers. Population and demographic data is derived from U.S. Census grids.

Armed with this information, the researchers drew one- and four-mile radii perimeters, or buffers, around the sites. The buffer radii are based on those used most frequently within scientific literature and by EPA's target distance limit in assessing potential adverse health effects from air and groundwater exposures.

"Using the actual footprint of the NPL site provides a more accurate estimation of potentially exposed populations," says Golden. "It's much better than other approaches, which draw concentric circles only from the center of the site, regardless of the site's actual shape."



*Urban and regional planner Meredith Golden  
(Photo courtesy of Meredith Golden)*



*The mapper allows users to zoom in for larger views of areas surrounding hazardous waste sites. (Graphic courtesy of Meredith Golden)*

## Addressing needs within the SRP community and beyond

This mapping application grew out of the recognition that, to improve public health, regulators responsible for cleaning up Superfund sites need to identify susceptible populations and evaluate their risks. These populations can benefit from focused educational and engagement activities. Recent technological advances allow for increasingly sophisticated applications of computer mapping and modeling techniques, so it is possible to identify the characteristics of populations living in proximity to the actual boundaries of sites.

One of the benefits of this map is the versatility of data input. “If one group has more detailed information for an area, it’s easy to add it in,” Golden said. The mapper can integrate new data provided by the EPA, USGS, or SRP centers from their ongoing work with individual sites. However, updates do require time and funding. Right now Columbia is working on adding new NPLs and updating the demographics with 2010 data.

The addition of analytical capabilities is next, according to Golden. Currently, users can visually compare results from several sites, but Golden would like to see a query feature that allows for more precise assessments. The researchers will also be making the jump to a JavaScript-based code to keep up with technological advances.

“Mapping applications can greatly benefit the assessment and remediation of Superfund sites,” says Golden. “I’m hoping that in the near future, NIEHS will host a mapping and data workshop for all agencies working on Superfund issues, so that we can coordinate our efforts and make the most of geospatial technology.”

Golden will share her data in the Partnerships for Environmental Public Health (PEPH) [webinar](#) titled “Mapping and Environmental Public Health: Visualizing Health Disparities” May 7, 12:00–1:30 p.m. EDT.

(Rebecca Wilson is an environmental health information specialist with MDB, Inc., a contractor for the NIEHS Superfund Research Program and Worker Education and Training Program.)

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## This month in EHP

*By Ian Thomas*

The federal government recently approved Shell’s oil-spill response plans for drilling in the Chukchi and Beaufort seas, setting the stage for exploratory drilling in the Arctic that could begin as early as July. The lead news story in the May issue of [Environmental Health Perspectives \(EHP\)](#) examines Shell’s plans for addressing oil spills in one of the most inhospitable regions on earth.

A second story, titled “Wrangling Reactive Nitrogen: Strategies for Mitigating Pollution,” discusses recent reports outlining proven methods for better managing the flow of reactive nitrogen into the environment from agricultural production, transportation, and electricity generation.

Finally, in this month’s [Researcher’s Perspective Podcast](#), host Ashley Ahearn sits down with guest Kathryn Cottingham, Ph.D.,



<http://twitter.com/ehponline>



to discuss her study of arsenic contamination in organic brown rice syrup, a common alternative to high-fructose corn syrup in some food products.

Featured commentaries, reviews, and research this month include the following:

- Arsenic, Organic Foods, and Brown Rice Syrup
- Climate Change, Migration, and Health
- Global Mortality and Smoke From Landscape Fires
- Mortality and Particulate Matter: A Canadian National Cohort Study

(Ian Thomas is a public affairs specialist in the NIEHS Office of Communications and Public Liaison.)

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## Extramural papers of the month

*By Nancy Lamontagne*

- [Health implications of temperature variability](#)
- [Autism risk linked to maternal diabetes and obesity](#)
- [Potential treatment for Parkinson's disease](#)
- [Environmental estrogens and developmental reprogramming](#)



Read the current Superfund Research Program [Research Brief](#). New issues are published on the first Wednesday of each month.

## Health implications of temperature variability

Climate change is expected to bring increasing variability in summer temperatures, which could shorten life expectancy for older people with chronic medical conditions, according to a new NIEHS-funded study. Although other studies have looked at the short-term effects of heat waves, this study examined the long-term effects of climate change on life expectancy.

The researchers used Medicare data from 1985 to 2006 to follow the health of 3.7 million chronically ill people over age 65. They studied whether mortality related to variability in summer temperature in 125 cities and took into account other factors, such as winter temperature variance, ozone levels, and individual risk factors. They compiled results for 125 individual cities and then pooled the results.

Within each city, years with larger summer temperature swings showed higher death rates than years with smaller swings. Each 1 degree Celsius increase in summer temperature variability increased the death rate for elderly with chronic conditions between 2.8 and 4.0 percent, depending on the condition. In addition, the researchers found the mortality risk was 1 to 2 percent greater for African Americans and those living in poverty and for African Americans, while the risk was 1 to 2 percent lower for people living in cities with more green space.

*Citation:* [Zanobetti A, O'Neill MS, Gronlund CJ, Schwartz JD](#). 2012. Summer temperature variability and long-term survival among elderly people with chronic disease. *Proc Natl Acad Sci U S A* 109(17):6608-6613. [Story](#)

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# Autism risk linked to maternal diabetes and obesity

New findings from the NIEHS-funded Childhood Autism Risks from Genetics and the Environment (CHARGE) study provide evidence that maternal metabolic conditions can increase the risk for autism, as well as developmental delay without autistic symptoms. The study suggests that fetal exposure to elevated levels of glucose and maternal inflammation adversely affect fetal development.

The metabolic conditions studied included obesity or hypertension at the start of pregnancy, or diabetes during pregnancy. Compared to normal-weight mothers without diabetes or hypertension, the researchers found that mothers who were obese were 67 percent more likely to have a child with autism spectrum disorder and more than twice as likely to have a child with another developmental disorder. Mothers with diabetes were also more than twice as likely to have a child with developmental delays as healthy mothers. In addition, children with autism spectrum disorder and diabetic mothers had greater deficits in adaptive communication, language comprehension, and language production than children with autism spectrum disorder born to healthy mothers.

*Citation:* [Krakowiak P, Walker CK, Bremer AA, Baker AS, Ozonoff S, Hansen RL, Hertz-Picciotto I.](#) 2012. Maternal metabolic conditions and risk for autism and other neurodevelopmental disorders. *Pediatrics*; doi: 10.1542/peds.2011-2583 [Online 9 April 2012].

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# Potential treatment for Parkinson's disease

NIEHS grantees report that the compound CLR01 successfully prevented the aggregation of alpha-synuclein in zebrafish without any toxic effects to healthy brain cells. The protein alpha-synuclein is thought to lead to Parkinson's disease when it aggregates in the brain and kills neurons, and CLR01 might offer a treatment for slowing or stopping the progression of the disease.

Since alpha-synuclein is found throughout the brain, it is challenging to find a drug that targets only the aggregates without destroying the protein's normal function. The researchers tested a novel molecular tweezer known as CLR01, which has been shown to inhibit the assembly and toxicity of proteins that have some similarities to alpha-synuclein.

They first experimented with CLR01 in cell cultures, finding that it kept alpha-synuclein from forming aggregates, prevented alpha-synuclein toxicity, and broke up existing aggregates. They also used fluorescent proteins to track CLR01's effect on the aggregations in a transgenic zebrafish model that expressed human alpha-synuclein in neurons and found that the molecular tweezer prevented alpha-synuclein aggregation and neuronal death.

*Citation:* [Prabhudesai S, Sinha S, Attar A, Kotagiri A, Fitzmaurice AG, Lakshmanan R, Ivanova MI, Loo JA, Klärner FG, Schrader T, Stahl M, Bitan G, Bronstein JM.](#) 2012. A novel "molecular tweezer" inhibitor of alpha-synuclein neurotoxicity in vitro and in vivo. *Neurotherapeutics* 9(2): 464-476.

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# Environmental estrogens and developmental reprogramming

An animal study by NIEHS grantees shows that environmental estrogens have distinct epigenetic effects in the developing uterus. The research provides insight into how early-life exposures to environmental estrogens can increase susceptibility to later development of hormone-dependent tumors.

The researchers studied the environmental estrogens genistein and bisphenol A (BPA), finding that genistein promoted the development of uterine fibroids in rats, while BPA did not. In the developing uterus, genistein and BPA both induce estrogen receptor signaling in a genomic manner, so how can they each activate the same receptor system but result in completely different outcomes?

The authors showed that genistein activated membrane-bound estrogen receptor via nongenomic mechanisms that were directly linked to pathways that caused histone phosphorylation. This histone phosphorylation reprograms estrogen-responsive genes in a way that makes them more responsive to hormones and increases the incidence of uterine fibroids later in life. However, BPA bound to the nuclear estrogen receptor without activating the membrane receptor and, therefore, did not activate the nongenomic histone phosphorylation pathway in the neonatal uterus. BPA, therefore, resulted in less estrogen-responsive gene expression in the adult uterus and no increase in uterine fibroids.

*Citation:* Greathouse KL, Bredfeldt T, Everitt JJ, Lin K, Berry T, Kannan K, Mittelstadt ML, Ho SM, Walker CL. 2012. Environmental estrogens differentially engage the histone methyltransferase EZH2 to increase risk of uterine tumorigenesis. *Mol Cancer Res* 10(4):546-557.

(Nancy Lamontagne is a science writer with MDB, Inc., a contractor for the NIEHS Division of Extramural Research and Training, Superfund Research Program, and Worker Education and Training Program.)

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## Intramural papers of the month

*By Anshul Pandya, Ian Thomas, and Darshini Trivedi*

- [Determining specificity for enzymes used in heparin and heparan sulfate production](#)
- [Calcium influx is a critical component of embryonic development](#)
- [Members of the Ccr4-Not complex crucial for embryonic stem cell circuitry](#)
- [Scientists link impaired lung development to Nrf2 deficiencies in neonatal mice under oxidant stress](#)

## Determining specificity for enzymes used in heparin and heparan sulfate production

NIEHS scientists have successfully crystallized an oligosaccharide substrate synthesized via an innovative chemoenzymatic approach, with the enzyme 3-O-sulfotransferase isoform 1 (3-OST-1). Sulfation by 3-OST-1 is the last step involved in the production of anticoagulant heparin and heparan sulfate. Heparin is an anticoagulant traditionally used to prevent the occurrence of blood clots, and recently has shown promise as

an anticancer and anti-inflammatory drug. Understanding the intricate interactions between sulfotransferases and their heparan sulfate oligosaccharide substrates provides a molecular foundation that can aid researchers in specifically engineering heparin for a variety of other purposes. Heparin derivatives would ideally be synthesized to function more efficiently, using lower dosages, and with fewer side effects.

Guided by multiple crystal structures of 3-*O*-sulfotransferases, multiple mutations were generated and analyzed for sulfotransferase activity and substrate binding specificity. Researchers discovered that in spite of structural similarities between the different 3-OST isoforms, these enzymes bind their substrates in different conformations. This work was performed in collaboration with investigators Jian Liu, Ph.D., from the University of North Carolina at Chapel Hill and Robert Linhardt, Ph.D., from the Rensselaer Polytechnic Institute. **(AP)**

*Citation:* [Moon AF, Xu Y, Woody SM, Krahn JM, Linhardt RJ, Liu J, Pedersen LC](#). 2012. Dissecting the substrate recognition of 3-*O*-sulfotransferase for the biosynthesis of anticoagulant heparin. *Proc Natl Acad U S A* 109(14):5265-5270.

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## Calcium influx is a critical component of embryonic development

Upon fertilization by the sperm, repetitive calcium oscillations occur as a result of the movement of calcium from egg storage or outside the cell, into the egg cytoplasm, and then back into storage or out of the egg. These calcium oscillations are essential for mammalian egg activation and the early stages of embryonic development. NIEHS scientists determined that some of the signaling pathways induced by calcium movements take place directly under the egg's plasma membrane, rather than entirely inside of the egg. The research has far-reaching implications, since defects in calcium signaling at fertilization can result in a failure of the embryo to implant or develop to term.

When mammalian sperm and egg first interact, a sperm-specific phospholipase, C zeta, contributes to the release of calcium from endoplasmic reticulum stores. Using a technique known as calcium insulation, the investigators induced persistent calcium oscillations in the egg cell while preventing an influx and efflux of calcium. In the absence of calcium influx, the fertilized eggs failed to undergo spindle rotation and emit the second polar body, thus resulting in the formation of three pronuclei, a fertilization abnormality. These studies have important implications for clinically assisted reproduction and fertility preservation technologies. **(DT)**

*Citation:* [Miao YL, Stein P, Jefferson WN, Padilla-Banks E, Williams CJ](#). 2012. Calcium influx-mediated signaling is required for complete mouse egg activation. *Proc Natl Acad Sci U S A* 109(11):4169-4174.

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## Members of the Ccr4-Not complex crucial for embryonic stem cell circuitry

NIEHS researchers have characterized the role of three key members of the Ccr4-Not complex within embryonic stem cell (ESC) self-renewal circuitry. The study demonstrates that Cnot1, Cnot2, and Cnot3, functioning as a protein complex, maintain self-renewal in both mouse and human ESCs, through the possible

inhibition of extraembryonic lineage differentiation. The work may provide valuable insight into mammalian embryonic development, and facilitate the use of ESCs in various drug and cellular therapies.

Using gene silencing along with a technique that they developed, the Oct4GiP reporter assay, the investigators showed that inhibition of Cnot1, 2, and 3 expression, not other components of the Ccr4-Not complex, led to significant differentiation of ESCs. The relative expression of Cnot1, 2, and 3, decreased during ESC differentiation and the silencing of these genes induced the expression of several early trophectoderm (TE) transcription factors.

These studies support the hypothesis that the complex maintains self-renewal by inhibiting TE transcription factors, thus preventing TE differentiation in mouse ESCs. Furthermore, these studies have identified that Cnot1, 2 and 3 have conserved functions in both mouse and human ESCs, and are important in the maintenance of both the naive and primed pluripotency state. **(DT)**

*Citation:* [Zheng X, Dumitru R, Lackford BL, Freudenberg JM, Singh AP, Archer TK, Jothi R, Hu G. 2012. Cnot1, Cnot2, and Cnot3 maintain mouse and human ESC identity and Inhibit extraembryonic differentiation. Stem Cells 30\(5\):910-922.](#)

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## Scientists link impaired lung development to Nrf2 deficiencies in neonatal mice under oxidant stress

A collaborative team, led by scientists at NIEHS, determined that Nrf2, a critical transcription factor involved in the body's protection against oxidant disorders, is essential for cell cycle and DNA repair, immune function, and antioxidant defense during postnatal normal lung maturation in mice. In addition, the researchers found a beneficial role for Nrf2 in hyperoxia-induced injury of undeveloped lung. The work has important implications for a wide range of oxidative stress-associated neonatal disorders, including bronchopulmonary dysplasia (BPD), a chronic lung disorder found in roughly 20 percent of low birth weight infants born each year in the United States.

Through the novel use of lung transcriptomics and pathway analysis, the researchers characterized complex gene expression networks in the saccular-to-alveolar stage transition during postnatal lung maturation. They also utilized microarray analyses to evaluate Nrf2-dependent defense mechanisms under normoxic and hyperoxic conditions in immature rodent lungs. Their studies found that newborn Nrf2(-/-) mice exposed to hyperoxia exhibited exacerbated pulmonary injury and DNA lesions, and were far more prone to an arrest of alveolarization than Nrf2(+/+) mice, implicating the importance of Nrf2. The results suggest a possible therapeutic role for Nrf2 in the protection of human BPD. **(IT)**

*Citation:* [Cho HY, van Houten B, Wang X, Miller-Degraff L, Fostel J, Gladwell W, Perrow L, Panduri V, Kobzik L, Yamamoto M, Bell DA, Kleeberger SR. 2012. Targeted deletion of Nrf2 impairs lung development and oxidant injury in neonatal mice. Antioxid Redox Signal; doi:10.1089/ars.2011.4288 \[Online 18 April 2012\].](#)

(Anshul Pandya, Ph.D., is an Intramural Research Training Award [IRTA] fellow in the NIEHS Laboratory of Neurobiology. Ian Thomas is a public affairs specialist with the NIEHS Office of Communications and Public Liaison, and a regular contributor to the Environmental Factor. Darshini Trivedi, Ph.D., is an IRTA fellow in the NIEH Laboratory of Toxicology and Pharmacology.)

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# Inside the Institute

## NTA meeting addresses accomplishments and concerns

By Eddy Ball

The [NIEHS Trainees Assembly \(NTA\)](#) held its spring 2012 general assembly meeting April 19 in Rodbell Auditorium, highlighting its accomplishments and plans for the upcoming year ([see text box](#)).

The trainees also took advantage of an opportunity to question NIEHS Scientific Director Darryl Zeldin, M.D., NIEHS/NTP Director Linda Birnbaum, Ph.D., and NIEHS Deputy Scientific Director Bill Schrader, Ph.D., about career development training needs, the potential impact of federal budget constraints on the Institute's training program, and, especially, progress toward hiring a fulltime director of the [NIEHS Office of Fellows' Career Development \(OFCD\)](#), vacant since the resignation of Diane Klotz, Ph.D., in 2011 ([see story](#)).

### Assurances from leadership

Moderated by NTA steering committee chair Tammy Collins, Ph.D., the meeting opened with remarks by Zeldin, who addressed questions submitted earlier, before opening the floor for additional questions from the audience. After reassuring trainees that any downsizing of labs, as a result of budget constraints, would honor the established protocol of giving affected trainees a one-year notice of termination, Zeldin moved to the topic of most concern to the trainees.

"We realize [that naming a head of OFCD is] a priority," Zeldin said, "and it has taken way too long ... Diane is missed, and we really need someone. We're working really hard to get it graded at the right level, so we can attract the best person and so we can keep them here."

He explained that to avoid any more delay caused by reclassification of the job, his office plans to use a contract mechanism in the very near future to provide for the needed tasks and duties, while continuing to complete filling the director position with a permanent federal employee. "We do not anticipate that this position will go away anytime soon."



Once Collins, above, Trivedi, and the other speakers began their presentation of what the NTA has planned, it was clear that trainees have accomplished a great deal, even in the absence of fulltime leadership of the OFCD. (Photo courtesy of Steve McCaw)



Zeldin told the trainees about the NIEHS Division of Intramural Research retreat on implementation of the Strategic Plan. "We have about a 21-page draft that is circulating through DIR now," he said, "and I'm hopeful that in the next week or two we'll be ready to roll that out [for division-wide comment]." (Photo courtesy of Steve McCaw)

When her time came, Birnbaum reinforced Zeldin's assurances about filling the OFCD position as quickly as possible. "We're convinced we can make this happen," she said. "That can happen quite quickly once we find the right person."

### Self-directed career development

"I am a big believer that part of your job as a trainee is to learn as much as you can, not only about your science, but what it means to be a scientist broadly defined," Birnbaum told the group. "My philosophy is, as a trainee, you want to spread your wings and fly ... to expand your horizons."

In response to a question about the Institute's commitment to education and outreach, Birnbaum underscored the importance of inspiring young people about science, technology, engineering, and mathematics careers, as well as the career development opportunities that outreach programs create for fellows.

Birnbaum also challenged trainees to seek out information about a range of careers in science, not just the careers they thought they'd have when they complete their postdocs. "None of you, no matter what kind of five- or ten-year plan you have, will be doing exactly what you think you'll be doing five or ten years from now."

### Planning and tracking progress for fellowship success

Schrader closed out the first part of the meeting with a discussion of trainee status reporting and renewal documents. "We put in process, a year ago, a document that's supposed to track what you're going to do when you get in the door and what the contract is between you and your boss," he said.

As Schrader explained, the reporting and renewal documents are important, because of the decentralized nature of training at NIEHS. Trainees and supervisors have the opportunity and obligation to specify expectations in writing, to protect both parties with the training agreement. An important component of the reporting process, he said, is the individual development plan beginning with the start of the fellowship. By documenting how well trainees meet their goals, the development plans help keep trainees and supervisors on track and figure into whether fellowships are renewed each year.



*"There are ways to do just about everything in the government," Birnbaum said about the drawn-out process of filling the OFCD position. "I tend to look for creative solutions." (Photo courtesy of Steve McCaw)*



*Heacock was one of several trainees who expressed concerns about the cost of daycare. Their special employment status as training awardees affects income tax credits, access to federal employee childcare subsidies, and other benefits. (Photo courtesy of Steve McCaw)*



*Schrader urged trainees to pay attention to the status and renewal documents that are used to evaluate performance. (Photo courtesy of Steve McCaw)*



*Closing out the meeting, Sarah Swerdlow, Ph.D., helped as Collins drew the names of winners for door prizes, ranging from coffee mugs to a copy of “Silent Spring” by Rachel Carson. (Photo courtesy of Steve McCaw)*

## NTA resources and upcoming events

Collins, co-chair Darshini Trivedi, Ph.D., and other speakers from the steering committee spent the final half hour of the meeting with an introduction of how the NTA serves the Institute’s 230 trainees, and an overview of career development and training opportunity resources.

Collins described the NTA office space in building 101, room F182 ([see story](#)) and the fellows’ listserv, a central communications hub for announcements, training opportunities, and job openings. She also urged trainees to get involved, by volunteering for NTA activities.

Filling in for coordinator Nisha Cavanaugh, Ph.D., and Mercedes Arana, Ph.D., Trivedi discussed outreach and teaching career development opportunities with the Citizen Schools Project ([see story](#)). Collins also gave an overview of the NIH [Summer Internship Program](#) at NIEHS and the Brown Bag Lunch series ([see story](#)), which features guest speakers, in a range of scientific careers, describing their work.

Michelle Heacock, Ph.D., took attendees through a long list of upcoming workshop and training opportunities. These range from the next open Grantsmanship Workshop in 2014 to weekly mentor training sessions to be held this summer. Additional planned opportunities include courses on conflict resolution, general writing, and scientific writing and publishing.

Ashley Godfrey, Ph.D., surveyed writing opportunities with the Environmental Factor [newsletter](#) and her own experiences as a guest writer. She then joined Trivedi in a description of the April 27 Biomedical Career Fair. Now in its 15th year, this year’s event will highlight recent postdoc alumni in panel discussions of careers ranging from faculty in teaching-intensive schools to small biotechnology firms, as well as foster networking.

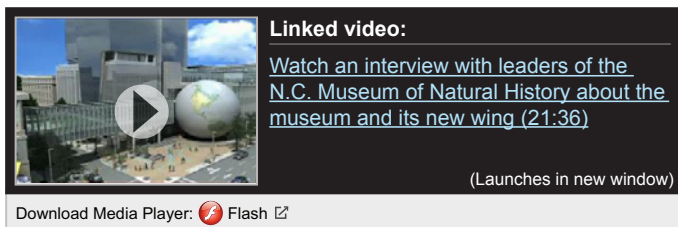
In closing the business section of the meeting, Collins highlighted the International Fellows Committee, fellows’ monthly coffee hour, and suggestion box, before ending with a drawing for door prizes.

For more information or to volunteer for NTA activities, contact Collins at [collinstr@niehs.nih.gov](mailto:collinstr@niehs.nih.gov) or Trivedi at [trivedidb@niehs.nih.gov](mailto:trivedidb@niehs.nih.gov).

# Outreach staff hits the pavement during NC Science Festival

By Eddy Ball

NIEHS outreach specialists joined the tens of thousands of people who flocked to downtown Raleigh, N.C., April 20-21 for the grand opening of the Nature Research Center at the [North Carolina Museum of Natural Sciences](#). Attended by an estimated 70,000 people, the 24-hour event was part of a 17-day statewide celebration of the [North Carolina Science Festival](#) April 13-29.



Specialists from the NIEHS [Office of Science Education and Diversity \(OSD\)](#), Ericka Reid, Ph.D., and Bono Sen, Ph.D., worked with volunteers from Institute labs to staff an information booth on environmental health. OSD used mechanical lung props, a setup for measuring lung capacity, and a poster, “Lungs, the Environment, and You,” from the NIEHS Citizen Schools project ([see story](#)), to underscore the importance of respiratory health.

Leading up to the grand opening ribbon cutting by N.C. Governor Bev Perdue was a parade that included a marching band from Raleigh’s Shaw University. Music and entertainment continued throughout the night and the next day, although most exhibitors worked their displays in shifts on Friday evening and Saturday.

Sen, who arrived well before the action began at 5:00 p.m., was talking with curious visitors even before she’d finished setting up the display. Foot traffic was brisk along the streets, which were closed to vehicles for the event, and the NIEHS team stayed busy interacting with people about environmental health and NIEHS research.



*The new \$56 million wing adds 80,000 square feet of display and laboratory space to the N.C. Museum of Natural History. Even before the additions, the museum was the top facility of its kind in the Southeast and the most visited museum in North Carolina. (Photo courtesy of Brian Russell)*



*Awe-inspiring displays in the museum’s main building have introduced generations of children and adults, K through gray, to the excitement of science. (Photo courtesy of Steve McCaw)*



*The NIEHS team and N.C. Science Festival Statewide Programs Coordinator Kathryn Fromson showed off the booth. Shown, left to right, Reid, NIEHS biologist Sylvia Hewett, her husband Steve, Fromson, Sen, and NIEHS biologist Huei-Chen Lao. Not shown: NIEHS biologist Tanya Whiteside. (Photo courtesy of Steve McCaw)*



*Burroughs Wellcome Fund communications staff Mindy McFeaters, left, and Russ Campbell gave out copies of the organization's new book for middle schoolers, "Science Explorers." Burroughs Wellcome was among some 75 nonprofits, governmental organizations, and educational institutions exhibiting at the event. A handful of scientific and environmental businesses also had booths along the streets. (Photo courtesy of Steve McCaw)*

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*Whiteside demonstrated lung function to some of the first visitors to the booth. (Photo courtesy of Steve McCaw)*



*Members of the parade that officially kicked off the grand opening set the tone for festivities that continued throughout the night and into the next day. (Photo courtesy of Steve McCaw)*



**NIEHS**  
National Institute of  
Environmental Health Sciences

NIH...Turning Discovery Into Health

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